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STUDIES IN EXPERIMENTAL SYPHILIS[1]

VIII. On the Localization of Syphilitic Lesions in Inflamed Areas

ALAN M. CHESNEY, M.D., THOMAS B. TURNER,[2] M.D., AND CHAS. R. L. HALLEY, M.D.

From the Department of Medicine of the Johns Hopkins University, and the United States Public Health Service

In a previous communication (1) from this laboratory evidence was brought forward to show that a granulating wound in the rabbit offers a particularly favorable site for inoculation with strains of *Treponema pallidum* virulent for the rabbit. When the surfaces of such wounds are inoculated with this microörganism the wounds heal, but subsequently a syphiloma makes its appearance in the scar and ultimately the wound breaks down again and a typical chancre develops. Sometimes these lesions attain huge proportions, and they can even be made to take on predetermined patterns.

This fact seemed so contrary to the generally accepted views concerning the resistance offered by granulating areas to bacterial infection that it seemed advisable to determine the behavior of such areas to other species of microörganisms, utilizing the same technic. For such a study, the results of which have already been reported (2), three varieties of microörganisms were employed; *Streptococcus erysipelatis*, *Staphylococcus aureus* and *Pasteurella avicida*. The experiments with these bacteria showed that granulating wounds in the rabbit offer a much higher degree of resistance to infection with streptococci and staphylococci than do fresh wounds. When these organisms were sown upon fresh wounds they produced an unmistakable local reaction, whereas upon granulating wounds little or no reaction was produced. When *Pasteurella avicida* was sown upon granulating wounds or fresh wounds no local reaction was elicited but in every instance the animal died. Inasmuch as this bacterium is highly virulent for the rabbit and

[1] Submitted for publication February 23, 1928.

[2] Jacques Loeb Fellow in Medicine.

uniformly kills that animal when inoculated subcutaneously, it is possible that it may have been necessary for only a very few of these organisms to make their way through the granulating wound in order to gain entrance to the circulation and bring about the death of the animal. The trauma incident to the removal of the crust before inoculating the granulating area may well have provided the necessary breach in what is otherwise a relatively resistant area, at least so far as some bacteria are concerned. At all events the experiments indicate that granulating wounds in the rabbit vary in their susceptibility to different types of bacterial infection; they appear to be resistant to direct infection with streptococci and staphylococci on the one hand, and susceptible to direct infection with syphilitic virus on the other.

This peculiar susceptibility of granulating wounds to syphilitic infection seemed worthy of further investigation because of its possible significance in the pathogenesis of human syphilitic lesions. As a first step in the solution of the problem it appeared desirable to determine whether areas in the body which were the seat of an inflammatory reaction were as susceptible to infection with syphilitic virus coming from within, as they are to that from without. To determine this point a series of experiments has been conducted in which inflammatory reactions were produced on the skin of the backs of rabbits and the animals subsequently inoculated either intratesticularly or intravenously with virulent strains of *T. pallidum*. The purpose of this communication is to record the results of these experiments. They may be said to show that treponemes in the circulating blood exhibit a marked tendency to localize in the inflamed area and to bring about the development of a syphilitic lesion at that point.

EXPERIMENTAL

All inoculations were made with the Nichols strain of *Treponema pallidum*. All the common breeds of rabbits were represented in the experiments.

Inflammatory areas were produced in the skin of the back of the rabbits exactly as in the experiments described in the previous papers, namely, by the excision of a rectangular area of skin under ether anesthesia. The area excised usually measured about 3 by 4 cm. Care was taken not to expose the fascia of the muscles, for if this happened,

delay in healing was encountered. The wounds were allowed to heal without any attempt, by surgical dressings or antiseptics, to prevent infection. In almost every instance the wound healed rapidly. Inoculations were made intratesticularly or intravenously either before or after the wound had completely healed. The protocols of the individual experiments follow.

Experiment 1. An area of skin was excised from the back of each of two male rabbits. Twenty-two days later each rabbit was inoculated intratesticularly with 0.1 cc. of a testicular emulsion containing virulent specimens of *Treponema pallidum*. At the time of inoculation the wound in each animal had completely healed. The subsequent course of events in these rabbits is described below. In all the protocols time is expressed in days after inoculation.

Rabbit no. 1643

Day of inoculation.	Wound healed.
21st day.	Orchitis, right.
48th day.	Orchitis, left. Indurated nodule in the scar of the wound, characteristic of syphilis.
55th day.	Indurated nodule in the scar has increased in size. Several other nodules in the scar.
60th day.	Lesions in scar larger. Skin papule on right foreleg. No lesions elsewhere.
67th day.	Lesions in scar beginning to heal.

Rabbit no. 1645

Day of inoculation.	Wound healed.
21st day.	Orchitis, right.
48th day.	Induration of scar on back. Left testis negative.
55th day.	Indurated area in scar larger. Positive for *T. pallidum*. Left testis negative. Sacrificed for autopsy.

Summary. In both rabbits orchitis appeared in the inoculated testis about the twenty-first day after inoculation and in both typical syphilitic lesions were manifest in the scars as early as the forty-eighth day of the disease. In one animal the lesion appeared in the scar at about the same time that the uninoculated testis showed evidences of syphilitic infection. In the other animal no lesion had appeared in the uninoculated testis up to the time of death.

Experiment 2. The foregoing experiment was repeated with a series

of three male rabbits, exactly the same technic being used. Twenty-seven days after excision of the skin on the back, each animal was inoculated intratesticularly with 0.2 cc. of a testicular emulsion containing virulent specimens of *T. pallidum*. The subsequent course of events in these rabbits was as follows.

Rabbit no. 1770

Day of inoculation.	Wound healed.
23rd day.	Orchitis and scrotal edema, right.
41st day.	Orchitis progressing. Scar violet red in color and contains several indurated areas; these are definitely syphilitic. Left testis negative.
49th day.	Orchitis receding. Left testis negative. Induration of scar increasing.
55th day.	Nodule in left testis. Two lesions in the scar, increasing in size.
71st day.	Right testis atrophic. Nodule in left testis larger. Lesions in the scar still present.
85th day.	Lesions on back subsiding.

No skin lesions appeared in this animal during the entire period of observation (205 days) except those which developed in the scar or just adjacent to it.

Rabbit no. 1773

Date of inoculation.	Wound healed.
23rd day.	Orchitis, right.
37th day.	Orchitis persists. Left testis negative. Extreme left end of scar is suspicious.
44th day.	Right testis smaller. Nodule in right scrotum. Left testis negative. Definite syphilitic lesion in left end of scar.
52nd day.	Scrotal lesion, right, subsiding. Left testis negative. Lesion in scar unchanged.
58th day.	Left testis negative. Scrotal lesion, right, subsiding. Lesion in scar subsiding. Small papule (syphilitic) adjacent to scar.
68th day.	Lesion in scar almost gone. Papule adjacent to the scar increasing in size. Left testis negative.
88th day.	All lesions healed.

Rabbit no. 1775

Day of inoculation.	Wound healed.
20th day.	Orchitis, right. Involved testis was excised for transfer of virus.

23rd day.	Left testis negative. Scar suspicious.
29th day.	Left testis negative. Scar still suspicious.
37th day.	Left testis negative. Scar still suspicious.
44th day.	Left testis negative. Definite syphilitic lesion in scar, treponemes demonstrated.
52nd day.	Left testis negative. Lesion in scar subsiding.
58th day.	Left testis negative. Lesion in scar healed. Animal discarded.

Summary. In all three animals syphilitic orchitis made its appearance about the twentieth day of the infection and in each of the wounds, which had healed at the time of inoculation, a syphilitic lesion made its appearance between the thirty-seventh and forty-fourth day after inoculation. In only one of the three animals did a syphilitic lesion develop in the uninoculated testis during the period of observation. No metastatic skin lesions, save those which developed in the scars or immediately adjacent to them, were observed in any of the three animals.

The foregoing experiments seemed to demonstrate conclusively that recently healed wounds in the rabbit constitute a favorable locus for the deposition of spirochetes following the inoculation of these microörganisms into the testis and their entrance into the circulation. In order further to analyze the phenomenon it seemed advisable to fix as precisely as possible the exact time at which the treponemes arrived at the wound. Obviously, if the inoculation were made into the testis, one could not be sure in any given case when the treponemes had gained access to the circulation, although it is known from the studies of Brown and Pearce (3) and of Kolle and Evers (4) that they make their way quickly into the adjacent lymph nodes following intratesticular or subscrotal inoculation. For this reason in the next experiment the inoculations were made intravenously and female rabbits were selected for study.

Experiment 3. An area of skin was excised from the back of each of a series of 4 female rabbits. Twenty-two days later a second area of skin on the back situated cephalad to the other was excised. At the time the second wound was made the first wound had healed in all but one of the rabbits. All 4 animals were inoculated intravenously 8 days after the second operation with 0.1 cc. of a testicular emulsion contain-

ing actively motile treponemes. In three of the rabbits at the time of inoculation the first wound had healed and the second was granulating and covered with a crust. In the fourth rabbit both wounds were still unhealed, but the older was naturally the smaller in size. Twelve rabbits inoculated subcutaneously with 0.1 cc. of the same virus emulsion at the same time served as controls and offered an opportunity, by study of the incubation period, to determine approximately the time at

FIG. 1. TWO SYPHILITIC LESIONS DEVELOPING IN WOUNDS ON BACK OF RABBIT NO. 1891, PHOTOGRAPHED 49 DAYS AFTER INTRAVENOUS INOCULATION

The margins of the lesions have been outlined in India ink

which the treponemes inoculated intravenously became localized in the inflamed area. The individual protocols follow.

Rabbit no. 1888

	First wound	*Second wound*
Day of inoculation.	Healed.	Granulating.
19th day.	Negative.	Healed. Scar suspicious.
27th day.	Scar suspicious.	Scar indurated, definitely syphilitic.

33rd day.	Definitely syphilitic nodule in scar. Excised for study.	Syphilitic nodule in scar.
41st day.	Second nodule at other end of scar.	Two syphilitic nodules in scar.
54th day.	Second nodule larger.	Both lesions ulcerating.
62nd day.	Nodule still increasing in size.	Both lesions larger.

Rabbit no. 1891

	First wound	*Second wound*
Day of inoculation.	Healed	Granulating.
20th day.	Scar indurated, definitely syphilitic.	Healed. Scar suspicious.
27th day.	Scar more indurated.	Scar slightly indurated, definitely syphilitic.
33rd day.	Induration increasing.	Entire scar indurated.
41st day.	Definite nodule.	Large syphilitic lesion.
49th day.	Nodule 1.5 cm. in diameter.	Chancre forming (see Fig. 1). Lesion of right ulna.
54th day.	Nodule larger.	Well developed chancre.

Animal autopsied and lesions saved for museum purposes. No lesion had developed elsewhere in the skin during the period of observation.

Rabbit no. 1893

	First wound	*Second wound*
Day of inoculation.	Healed.	Granulating.
19th day.	Scar suspicious.	Healed. Scar indurated. definitely syphilitic.
27th day.	Scar indurated, definitely syphilitic.	Scar indurated.
33rd day.	Induration increased. Lesion excised.	Induration increased. Lesions excised.

No lesion had developed elsewhere than in the scar during the period of observation.

Rabbit no. 1894

	First wound	*Second wound*
Day of inoculation.	Granulating.	Granulating.
19th day.	Granulating	Granulating.
27th day.	Granulating.	Not completely healed. Healed portion suspicious.

33rd day.	Healing slowly.	Scar definitely indurated.
41st day.	Almost healed.	Typical syphilitic lesion.
49th day.	Healed.	Lesion larger.
54th day.	Negative.	Huge lesion, ulcerating.
62nd day.	Negative.	Huge chancre.
67th day.	Scar indurated, violet in color. *T. pallidum* present.	Chancre persists (Fig. 2).

FIG. 2. TWO SYPHILITIC LESION DEVELOPING IN WOUNDS ON BACK OF RABBIT NO. 1894, PHOTOGRAPHED 67 DAYS AFTER INTRAVENOUS INOCULATION

The margins of the lesions have been outlined in India ink

No lesions developed elsewhere than in the scars during the period of observation.

Controls. In each of the 12 control animals inoculated subcutaneously at the same time with 0.1 cc. of the same virus emulsion a lesion appeared at the site of inoculation. The incubation period of these lesions varied from 19 to 27 days.

Summary. In each of the healed or granulating wounds of the four test rabbits syphilitic lesions made their appearance at varying inter-

vals after inoculation; 19 days in 1, 20 days in 1, 27 days in 3, 33 days in 2 and 67 days in 1 animal. Some of these lesions attained a relatively large size. In one of the animals a metastatic bone lesion was observed, but in none of them were skin lesions observed other than those which developed in the scars. In the control animals inoculated subcutaneously, lesions developed at the site of inoculation in every instance, at intervals of 19 to 27 days following injection. The close parallelism between the incubation period of the lesions in the two groups of animals suggests that in the case of the animals inoculated intravenously the scars became infected very shortly if not immediately after inoculation.

In all of the foregoing experiments the wounds, if not healed at the time of inoculation, became completely so before the syphilitic lesion made its appearance. The evolution of these lesions was characteristic and uniform. The first sign indicative of the presence of syphilitic infection was that the scar took on a distinctly violet red color. About the same time, or a little later, the scar would become definitely indurated, either in one portion or throughout its entire extent. From that time on the induration became more marked, and the skin elevated and redder in color. A little later necrosis appeared in the central portion of the scar and the lesion would then usually progress until a typical chancre was formed. Sometimes two lesions would develop almost simultaneously and perhaps fuse, giving rise to an unusually large lesion. It was striking to see how the syphilitic inflammatory reaction followed the line of the scar, that is to say, of the previous non-specific inflammatory reaction. It was no uncommon sight, when a wound had left a stellate scar, to see the syphilitic lesion take on the same stellate pattern in its early stages, which however was apt to be lost as the lesion attained its maximal size. It was not always easy to determine precisely, from clinical observation, the day on which the syphilitic lesions appeared in the scars, and no consistent attempt was made to determine it by search for treponemes in the lesion, since we wished to avoid doing anything to the latter which might conceivably retard or hasten its development. However, in those instances where the suspected lesions were examined for *T. pallidum* very early, these organisms were usually found in such numbers as to convince one that they had been present for some time and that the first sign of increasing

induration in the scar could be taken as a reliable clinical index of the presence of syphilitic disease.

CLINICAL OBSERVATIONS

The foregoing experiments leave little doubt as to the susceptibility of inflamed areas in the skin of the rabbit to infection with the syphilitic virus, and the tendency of syphilitic lesions to develop in these areas. While the subject has been under experimental investigation, opportunity has been afforded us to observe, in 2 patients in the Syphilis Clinic of the Johns Hopkins Hospital, what we believe to be two natural experiments which illustrate the same phenomenon. Both occurred in negroes who had had previous injuries and not long thereafter had acquired syphilis. In each instance syphilitic lesions developed in the areas where there had previously been an injury. The histories of these patients follow.

Case 1. H. G. No. H 59001. Colored, female, 22, married, waitress.

January, 1927. The patient burned both forearms and left upper arm slightly by coming in contact with a steam pipe. These burns were not severe enough to bring her to the hospital.

February 16, 1927. Came to the Gynecological Dispensary on account of metrorrhagia. No lesions on external genitalia.

March 16, 1927. Came to Dermatological Dispensary on account of "pimples on the face." Diagnosed "acne." Wassermann suggestive negative (+).

May 3, 1927. Came to Surgical Dispensary because her old burns were bothering her. Examination showed: "Chronic ulcer on flexor surface of left forearm, surrounded by a few pustules; on the other arm she has several raised areas, also on the left chest. They are rather suggestive of lues." The patient was referred to the Syphilis Clinic but did not report there until 6 weeks later.

June 25, 1927. Admitted to the Syphilis Clinic. Physical examination revealed: Kerato-iritis, condyloma in right axilla, several pigmented annular lesions on trunk resembling healed syphilitic lesions, palmar and plantar syphilides, numerous condylomata on external genitalia. On the flexor surface of the left forearm and on the dorsal and flexor surfaces of the right wrist and on the right arm near the elbow there were the remains of the old burns. The first three of these were covered with a thin crust, the one on the arm was completely healed but pigmented. On removal of this crust in each instance a clean grayish-red smooth moist area was exposed. It was not ragged and did not bleed easily. It was not painful. In appearance it suggested syphilis (Figs. 3, 4). Serum obtained from each of these three lesions and examined by dark field illumination showed the presence of typical examples of *T. pallidum*. Serum obtained from

the condyloma in the axilla also showed the presence of *T. pallidum*. The blood Wassermann was positive. Following the administration of arsphenamine intravenously all the lesions including those at the site of the old burns healed promptly.

Comment. In this instance it seems fairly clear that the patient received her burns before she acquired her syphilis. At any rate, the

FIG. 3

FIG. 4

FIG. 3. FOREARMS OF PATIENT H. G., SHOWING SYPHILITIC LESIONS DEVELOPING IN RECENTLY BURNED AREAS

Serum from these lesions positive for *T. pallidum*

FIG. 4. AXILLARY LESIONS OF SAME PATIENT (H. G.), SHOWING CONDYLOMA, SERUM FROM WHICH SHOWED T. PALLIDUM

syphilitic lesions did not appear until after she had been burned and it is noteworthy that she did not seek the advice of physicians for her burns until 4 months after the injury, when they began to give her trouble. One cannot of course dismiss the possibility that the burned areas were inoculated by the patient herself with material from her syphilitic lesions, but this possibility seems rather remote, since purposeful auto-inoculation during the secondary stage, as a rule, yields

negative results. We incline to the view that in this instance the burned areas were infected with syphilitic virus coming by way of the blood-stream and not from without.

Case 2. M. R. H 28045. Colored male, single, 21. Admitted to the Syphilis Clinic July 23, 1925, on account of a "breaking out." Between 1 and 2 years previous to admission he had been cut with a razor while in a fight. Wounds had been inflicted on the left side of the face and also on the trunk and right arm posteriorly. These healed with the formation of keloids.

FIG. 6 FIG. 5

FIG. 5. SYPHILITIC LESIONS ON THE SIDE OF FACE WHERE THERE WERE NO SCARS

FIG. 6. SYPHILITIC LESIONS ON THE SIDE OF FACE WHERE THERE WERE KELOID SCARS

Note the tendency of the lesions to appear along the keloids

Six months prior to admission a single hard small sore appeared on the penis. He was given 2 injections of arsphenamine by his physician and the sore healed promptly. Five months later, or one month prior to admission, "spots" appeared on the face and trunk.

Physical examination. Profuse papular syphilide involving the trunk but principally the face. Many lesions annular in type. *Marked tendency for the lesions to be grouped along the keloid scars* (Figs. 5, 6, 7). Indurated scar at urethral orifice, the site of the former genital lesion, according to the patient.

Blood Wassermann ++++. The patient disappeared after one injection of neoarsphenamine and could not be traced.

Comment. While the precise date of infliction of the lacerations could not be ascertained, it is certain that they occurred prior to the

FIG. 7. SYPHILITIC LESIONS ON THE TRUNK AND RIGHT ARM
Note the tendency of the lesions to appear along the keloids

onset of the syphilis. That the lesions which developed along the line of the scars could have been the result of auto-inoculation seems out of

the question, because from their size and appearance they were manifestly of the same age as the skin lesions located elsewhere, which had been present only a month.

The sequence of events in these two patients demonstrates to our minds that, in the human being, areas of the skin that have been the seat of a comparatively recent inflammatory reaction resulting from trauma constitute favorable sites for the localization and development of syphilitic lesions, if and when the individual subsequently acquires syphilis. The intimate relationship of trauma and the occurrence of syphilitic lesions has long been known (see review by Klauder (5)), but for the most part the observations have dealt with the occurrence of late lesions (gummata) in patients already syphilitic and in whom special areas were subjected to trauma operating late in the course of the disease. Much less attention has been paid to the development of syphilitic lesions in areas of the skin that have been traumatized shortly before the patient acquired syphilis, although observations by Dohi (6) and by Keidel and Zimmermann (7) show conclusively the susceptibility of tattooed areas of the human skin to the localization and development of syphilitic lesions. These authors made the interesting observation that the syphilitic lesions were prone to develop in tattooed areas where pigments other than those containing mercury (cinnabar) were deposited; but that no lesions developed in the red area in which cinnabar was the pigment used. These findings were confirmed experimentally by Asoki (8). It seems not unlikely that the localization of syphilitic lesions in tattooed areas of the skin is determined by the same mechanism which brings about their localization in recent scars, both in rabbits and in human beings, whatever that may be.

DISCUSSION

The experiments show clearly the susceptibility of recently healed and granulating wounds of the rabbit to infection with virulent strains of *Treponema pallidum* introduced either into the testis or directly into the circulation. This susceptibility seems to be quite as marked toward syphilitic virus coming from within as toward that introduced from without. The case histories indicate that the same state of affairs obtains in human beings.

The reason why a non-specific inflammatory reaction, such as occurs in a recently healed or a granulating wound, offers a favorable site for the localization and development of syphilitic lesions is by no means clear. In a former communication (1) it was suggested that such areas may offer more favorable opportunities for the growth of treponemes, possibly due to an abundant food supply. This suggestion was brought forward because upon study of the histology of these granulating wounds at the time of inoculation we were impressed with the evidence of cellular activity in these areas as manifested by the large number of new cells. Study of sections of the healed wounds in the rabbits in the third experiment, taken at the time of intravenous inoculation, and hence presumably that of localization of the spirochetes, showed that the acute inflammatory reaction had largely subsided and new connective tissue was apparently no longer being formed, although the cells of the epithelial layer were still numerous and large and there were many blood vessels present. In other words, these healed wounds had not yet reached the end-stage of inflammation and were by no means avascular.

It is possible that the phenomenon may be explained upon a purely anatomical basis, such as an increase in the number of capillaries or a pinching off of the same, or upon the basis of changes in the rate of flow of the blood through the inflamed area, or again, upon increased permeability of capillaries in this region. We have not as yet sufficient data upon these points to permit the formulation of any precise views. An adequate explanation will have to await further studies which are now in progress. More particularly it will be desirable to determine how long a scar remains susceptible to syphilitic infection and whether an inflammatory reaction of less degree, in which there is no destruction of the superficial layers of the skin, will prove to be as susceptible to syphilitic infection as one of greater degree, in which there has been a break in the continuity of the epithelium. In this connection we have interesting data indicating the susceptibility to syphilitic infection of inflamed areas of the skin produced by the application of coal tar, but these studies are as yet in the initial phase only and require amplification. It is possible that the principle illustrated by the experiments outlined above may provide a method for the production of lesions of the viscera in rabbits, and experiments dealing with this possibility have been projected.

SUMMARY AND CONCLUSIONS

A series of experiments has been performed in which rabbits with either healed or granulating wounds (or both) upon their backs were subsequently inoculated intratesticularly or intravenously with a virulent strain of *Treponema pallidum*. In each instance syphilitic lesions developed in the scars of the wounds. These lesions exhibited a marked tendency to conform to the pattern of the scars. The incubation period of the lesions developing after intravenous inoculation corresponded closely with that of lesions which developed at the site of inoculation after subcutaneous injection. From this it is inferred that shortly or immediately following intravenous inoculation the treponemes reach the scar and are deposited there.

The histories of two patients are presented, in whom syphilitic lesions developed in previously traumatized areas of the skin, when the syphilitic infection was acquired subsequent to the injury.

It is concluded that recent non-specific inflammatory reactions of the skin of both rabbits and human beings, resulting from wounds, constitute foci favorable for the lodgement and growth of the *Treponema pallidum* coming from within the body, and predispose to the evolution of syphilitic lesions in those areas.

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THE TUBO-UTERINE JUNCTION IN VARIOUS ANIMALS[1]

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INTRODUCTION

In 1925 two short preliminary notes were published to call attention to the morphology and the possible physiological function of the anatomical structures at the uterine opening of the Fallopian tube. At that time it was noticed that it was sometimes easy to force India ink from the uterus into the tube, while at other times the wall of the uterus would rupture before any injection mass would enter the tube. In a search for an explanation, a routine histological study was made of the region marking the junction of tube and uterus in the ordinary laboratory mammals, and as indicated previously, special structures were found which might help to explain the varying patency of this region. Accordingly, the purpose of this article is to set forth in more detail the anatomy of the uterine ostium of the Fallopian tube in those animals whose organs are commonly studied in the laboratory.

MATERIAL AND METHOD

Unless otherwise specified all the material was obtained from laboratory animals that were killed with ether. The material was fixed as quickly as possible after the uterine injection. In several instances it was felt that a distended uterine cornu, when injected with a fixing fluid and later fixed in the same fluid, would give a better idea of the anatomical structures, particularly with a view to showing their relationship when subjected to pressure, than would the ordinary non-injected uterus. For instance, it was learned incidentally that the mucosa of the pig's uterus would frequently be in such folds that in such an injected and distended uterus a fold might extend almost completely across the lumen.

[1] Received for publication February 17, 1928.

Guinea-pig. The material was obtained from a small young female guinea-pig weighing 270 grams. The animal was not pregnant, and it was not until a pressure of 30 mm. of mercury was reached in the injection of the uterine cavity that any ink entered the Fallopian tube. However, even with this pressure only a small amount entered the tube, as was evidenced by traces of this injection mass at the ampulla, as well as by the examination of sections of the Fallopian tube which showed only a small amount of ink within the

FIG. 1. × 8. Longitudinal section of a guinea-pig uterus, *a*, to show the coils of the Fallopian tube, *t*, and its entrance into the uterus near the region *b* which is enlarged in the next figure. In this case the tube enters virtually at the apex of the uterus where a thickening of its wall exists.

lumen of this structure (*t*, Fig. 1). The tube joined the uterus almost at the very apex of the cornu (*b*, Fig. 1). Examination of the uterus showed that its musculature was arranged essentially in the fashion of a closely wound spiral. The entire block of tissue, containing the terminal portion of the cornu of the uterus, with tube and ovary was fixed in Bouin's fluid, sectioned serially in celloidin, and stained with Van Gieson and iron hematoxylin stains.

Microscopic examination showed that the junction of tube and

uterus was characterized by a slight elevation within the uterine cavity (Fig. 2). This elevation was not marked by any gross structures, such as polypoid projections as seen in the rabbit and pig, but it was essentially an increase in the stroma layer. The epithelial cells covering this elevation, except for being slightly more columnar,

FIG. 2. × 90. Guinea-pig uterus; a magnification of the region *b* in Figure 1. The lumen of the tube, *b*, is in direct communication with the uterine cavity, *a*. The stromal layer is thick here and contains uterine glands, *g*, almost up to the tubal ostium. Although the section is cut longitudinally to the axis of the tube, a marked thickening of the musculature, *m*, is evident, indicating a possible sphincter action.

resembled the epithelial cells lining the main portion of the uterine cavity. The epithelial cells of the tube were still more columnar. Many of the lumina of the uterine glands within this elevation contained some of the ink which had been injected within the uterine cavity. The stroma cells were packed more densely near the tubal

ostium than elsewhere. In this region also, as mentioned above, this stromal layer had the greatest depth, being easily five times as deep as the corresponding layer in the main body of the uterus. Of particular interest was the large amount of plain muscle tissue, chiefly circular in arrangement, which guarded the tubal ostium like a sphincter (*m*, Fig. 2). That this increase in plain muscle is absolute,

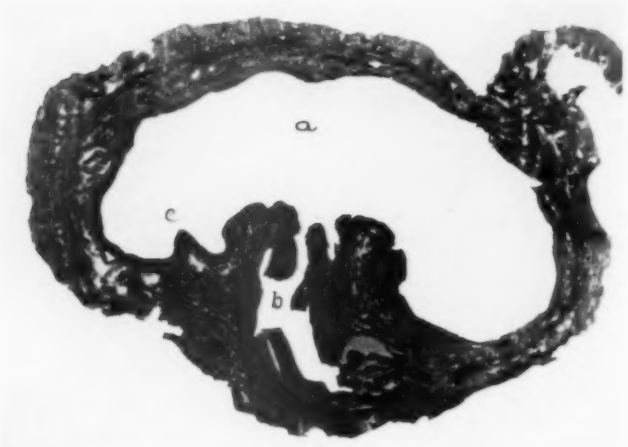

FIG. 3. × 80. Cross-section of uterus of a white mouse showing the entrance of the tube, *b*, into the uterine cavity, *a*, near the apex of the cornu. In this region the mucous folds guarding the tubal ostium are markedly developed, and one, *c*, is situated quite laterally. Any distention of the uterine cavity might easily compress these folds over the tubal opening and effectively block this passage.

and not due to a tangential section of the muscle layer, is obvious from the fact that the section is through the axis of the terminal portion of the tube. A few lymph vessels were seen in the periphery of this muscular layer, and only rarely did these vessels penetrate more deeply into the wall of the uterus.

Mouse. The specimen was obtained from an adult female white mouse that was killed with ether. The animal was not pregnant.

Bouin's fixing fluid, which was injected into each cornu of the uterus, soon appeared in the ampulla of the tube. It was evident that the tube joined the uterus almost at right angles near, but not at, the apex of the cornu. Both cornua were serially sectioned in paraffin at a thickness of six micra, and stained in Mallory's connective-tissue stain. One cornu was sectioned transversely to its axis, the other was cut longitudinally.

Both specimens showed the same general morphological structure. In brief, the entrance of the tube into the uterus was marked by a very definite mound-like protrusion, as if the end of the tube were

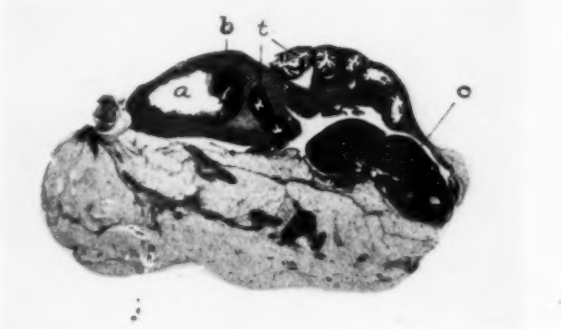

FIG. 4. × 8.3. Section of uterus, tube and ovary of rat. The uterine cavity is represented by *a*, the tube with its many convolutions by *t*, and the ovary by *o*. The area *b*, marking the entrance of the tube into the uterus, is enlarged in Figure 5.

partly inverted into the lumen of the uterus (Fig. 3). Through the center of this projection the tube entered. The epithelium at the tubal ostium resembled more that of the tube than that of the uterine cavity. No glands were seen in this protruding structure in which the stroma cell layer was increased in thickness, but less compact than elsewhere. A slight increase in the circular muscle at the tubal ostium, as well as a blood supply better than in the adjoining tube or uterus, was noted. It was difficult to determine with any degree of certainty the amount of lymph supply to this region; however, it was insignificant in comparison with the large supply found in the rabbit and pig.

Rat. An adult female rat, that was not pregnant nor in oestrus was injected with India ink into the right uterine cornu. The intrauterine pressure was controlled with a mercury manometer, and even when the pressure reached 250 mm. of mercury no ink entered the tube. While this pressure was being maintained, the uterus was

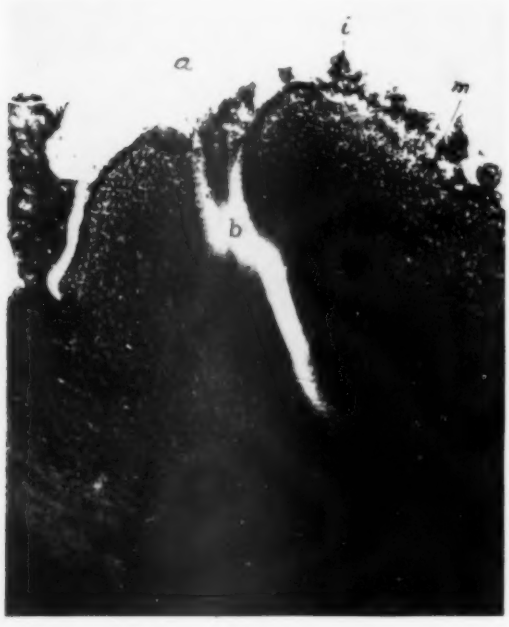

FIG. 5. × 120. Tubo-uterine junction of rat; an enlargement of *b*, Figure 4. Again, a mound-like elevation marks the entrance of the tube, *b*, with the uterine cornu, *a*. The increased circular plain muscle, *m*, suggests a sphincter action. Apparently the ink, particles of which, *i*, are in the uterus, never entered the tube.

ligated and placed in Bouin's fixing fluid. The specimen was subsequently serially sectioned in celloidin and stained with iron hematoxylin and Van Gieson stains.

As will be seen from Figure 4, the tube joined the uterus in a manner similar to that found in the white mouse, that is to say, the juncture

was not at the very apex of the cornu, but slightly below this point. A definite elevation in the uterine cavity, conical in character and again similar to the one found in the white mouse, was present at this ostium. The epithelium lining this elevation was slightly different from that found in the neighboring uterine cavity and tube, in that the individual cells were cuboidal and contained only a little cytoplasm. Particles of India ink were present at the very ostium of the tubal

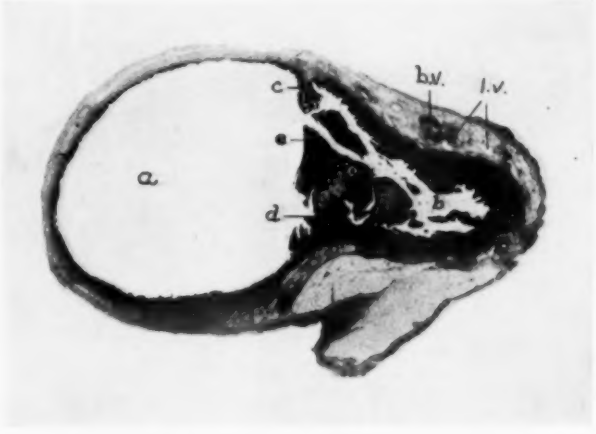

FIG. 6. × 7.7. Section of the pregnant uterus of a rabbit. At the junction of the tube, *b*, with the uterine lumen, *a*, several projecting folds, *c* and *d*, are seen which partially block the tubal ostium. A bit of fetal membrane is at *e*. Blood vessels, *b.v.*, and lymph vessels, *l.v.*, are recognizable. The marked thickness of the muscle layer at *d* is given in greater magnification in Figure 7.

orifice (Fig. 5), but none of this injection mass had entered the tube. The stroma layer was again relatively thick, and the individual stroma cells were less compact than those in adjoining areas of the uterus. One of the striking features was the large amount of circular muscle at the tubal ostium (*m*, Fig. 5). The blood supply to this general region was good, but not unusually so. Only a few small vessels, apparently lymphatic in character, were seen.

Rabbit. In the rabbit one could detect with the unaided eye the

presence of numerous polyp-like masses within the cavity of the uterus at the tubal ostium. With a hand lens from twelve to eighteen of these projections were readily counted; they formed a compact mass, which occupied completely the opening of the tube. After the uterus was opened longitudinally at this point, the individual polypoid

FIG. 7. × 90. Rabbit uterus; enlargement of area *d* in Figure 6. The base of a mucous fold is represented as situated between the uterine cornu, *a*, and the tube, *b*. The stromal layer is indicated by *s*. At the base of this layer is a well defined circular layer of plain muscle, *m*, having numerous lymph vessels, *l.v.*

masses had two or more smaller protrusions on them. The average length of these large projections was about 1.2 mm. In this animal also the tube joined the cornu of the uterus obliquely (Figs. 6 and 8). In the specimen shown in Figure 8, ink did not pass into the tube until a pressure of 60 mm. of mercury had been reached.

Microscopically, the polypoid projections were covered with ciliated columnar epithelium which was virtually identical with the epithelial lining of the tube; the uterine epithelium was relatively more cuboidal. Only a few glands were seen, and these were at the base of the most lateral projections. The bulk of each protrusion was made up of loose connective tissue which contained an average number of blood and lymph vessels. The plain muscle layers, chiefly the circular, were

FIG. 8. × 40. Uterus of a rabbit. The animal was not pregnant. The tube, *b*, enters the uterus, *a*, obliquely. At this junction there are numerous polyp-like projections, *c*, some of which are continuous with the longitudinal folds within the tube. The circular muscle is prominent at *m* and m^1.

definitely increased at the tubal ostium (Figs. 7 and 8). In this respect a specimen obtained from a pregnant uterus was of particular interest; for in this case, as is shown by Figure 6, some of the polypoid masses were made to project well into the lumen of the tube. One of these masses was particularly large, and its base rested on a marked elevation of circular muscle (Fig. 7). Examination of serial sections of this region showed that this marked increase in circular muscle was not always capped by a polypoid projection, but was well within the

uterine cavity for a portion of its extent. A peculiar feature of this specimen was that this bit of circular muscle was markedly developed only for about a half of the tubo-uterine juncture. In Figure 8, taken from a non-pregnant uterus, the circular arrangement is well represented on both sides of the tubal lumen. Again the blood supply to this part of the tube and uterus was unusually abundant. Lymph vessels were present in great numbers within the polypoid masses, plain muscle and adventitia.

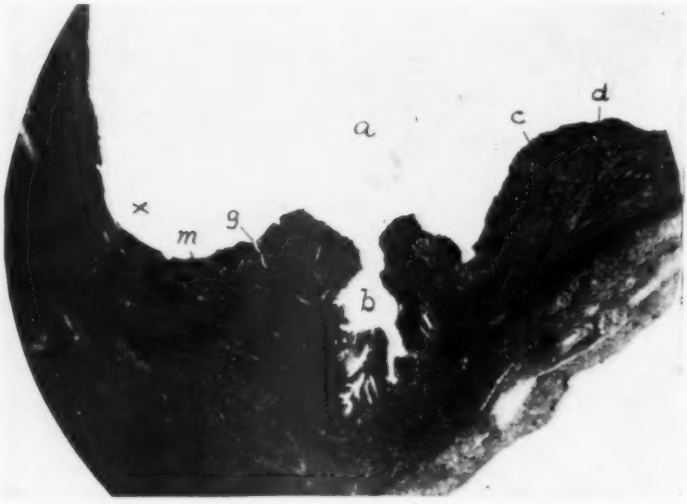

FIG. 9. × 50. Uterus of a cat. The tube, *b*, joins the cornu, *a*, obliquely near the apex, *x*. At this junction are several folds, some of which have glands, *g*, near the ostium, whereas others, *c*, have the uterine glands limited as at *d*. The circular muscular layer at *m* is well developed.

Cat. At the end of a sacrifice experiment on an adult non-pregnant cat, India ink was injected into the right cornu of the uterus in the direction of the tube. Since no ink escaped into the abdominal cavity even though considerable pressure was exerted upon the syringe, it was decided to investigate the reason why no ink entered the tube. The tubo-uterine juncture, which showed that the tube joined the uterus obliquely, was fixed in Bouin's solution and sectioned serially

in celloidin. This animal gave the first clue as to the mechanism which prevented the injection of the lumen of the tube.

Examination of the sections showed that there was a definite elevation within the uterine cavity at the point where the tube entered (Fig. 9). Through the center of this elevation the lumen of the tube continued, and opened in an irregular fashion near the apex of this more or less regular protrusion. The mound-like mass, *d*, in this figure was shown by a study of the serial sections to be an elaborate extension of one part of the elevation. The epithelium lining this elevation was a transition form between the relatively flat cells of the uterine mucosa and the more columnar cells lining the tube. Uterine

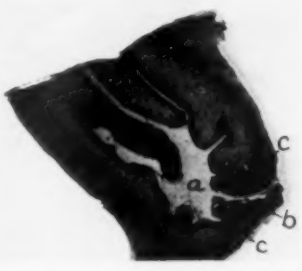

FIG. 10. × 4.1. Section of the uterus of a dog to show the oblique entrance of the tube, *b*, near the apex of the uterine cornu, *a*. The two folds, *c*, at this point are enlarged in Figure 11.

glands were seen mainly at the peripheral portion near the base; a few structures resembling large uterine glands, *g*, were observed only on one side of the elevation. The stroma layer was relatively dense in this elevation, and contained a large amount of fibrous connective tissue. The plain muscle, particularly the circular band of fibers, was well developed, and again suggested a sphincter activity. A good blood supply to this general region was noted; lymph vessels were few and small.

A wax-plate reconstruction was made of this specimen, but since Figure 9 shows the essential features of this specimen no further illustrations were deemed necessary.[2]

[2] This wax plate reconstruction, as well as the taking of the photograph for Figure 14, was made possible through the coöperation of Dr. George L. Streeter, of the Department of Embryology, Carnegie Institution, Washington, D. C.

Dog. The specimen was obtained from an adult non-pregnant female dog whose uterus was large and firm, suggesting an early premenstrual state. India ink was injected into one of the cornua, and although considerable pressure was used, no ink escaped through the tube. As shown in Figure 11, particles of ink are present at the very

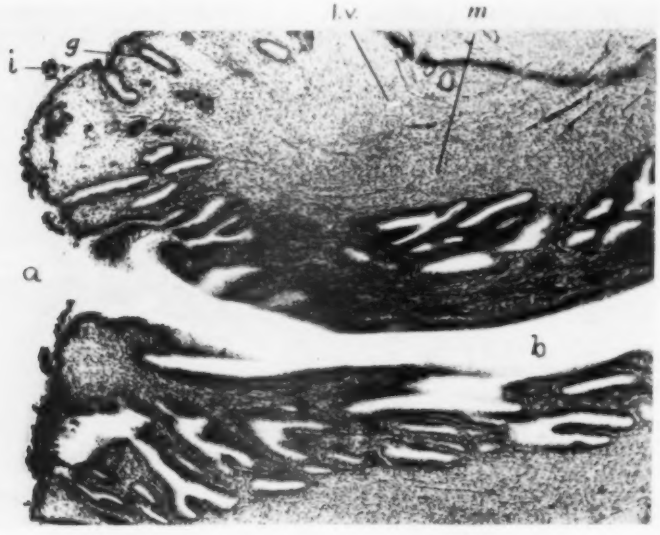

FIG. 11. × 70. Enlarged photograph of the tubo-uterine junction of the dog as given in Figure 10. The tube *b*, enters the uterus at *a*. Uterine glands, *g*, are near this point. The plain muscle layer, *m*, is increased and is supplied by a moderate number of lymph vessels, *l.v.* Although ink was injected into the uterine cavity under pressure, some ink particles, *i*, are seen on the uterine epithelium, but none have entered the tube.

tubal ostium, but none are found in the lumen of the tube, thus indicating that the lumen was closed. The tube joined the uterus obliquely and not at the very apex of the cornu (Fig. 10). This juncture, together with the ovary and tube, was fixed in Bouin's solution.

It was seen (Fig. 10), that there were numerous large folds and mucous projections at the apex of the cornu, and the protrusion which

marked the entrance of the tube was not more conspicuous than the others. The ciliated epithelium at the tubal ostium was highly columnar and resembled more the epithelium of the tube than the slightly less columnar epithelium of the uterine cavity. Uterine glands were present almost to the very opening of the tube. The stroma cells were very loosely arranged at the extremity of the mucous projections; however, they were more densely packed at the base where fibrous connective tissue was also more in evidence. Plain muscle tissue, particularly in the circular layer, was well developed

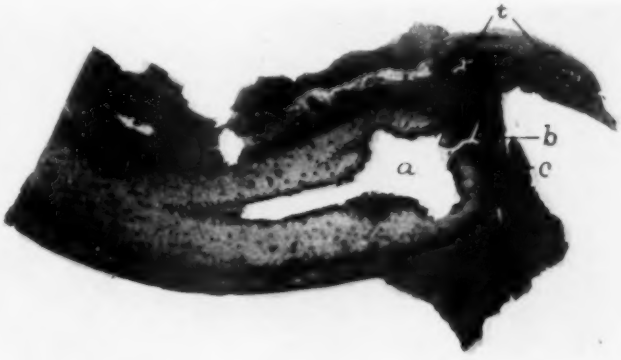

FIG. 12. × 5. Section of the uterus of a young lioness. The tube, *t*, with its numerous convolutions joins the uterus, *a*, obliquely. A slight mucous fold is at *c*. The area *b* is enlarged in Figure 13.

(Fig. 11) and appeared to sweep down with the corresponding layer of the tube. The usual good blood supply was present in this region; but the lymph vessels were small and few.

Lion. It is obviously difficult to include the lion in the group of laboratory animals. However, it happened that a female lion cub which was born and raised in the local zoological park, after having reached the age of one and a half years, developed a deformity of the legs, not unlike rickets, which made the animal unfit for exhibition purposes. About two hours after the animal had been killed with potassium cyanide it was possible to obtain the reproductive organs.

India ink was injected into the left cornu of the uterus, and although great pressure was exerted upon the syringe, no ink escaped from the tube; subsequent histological examination failed to show any ink within the lumen of the tube, (Fig. 13). With the uterine cavity still under pressure the tubal end of the uterus was fixed in formalin and sectioned serially in celloidin.

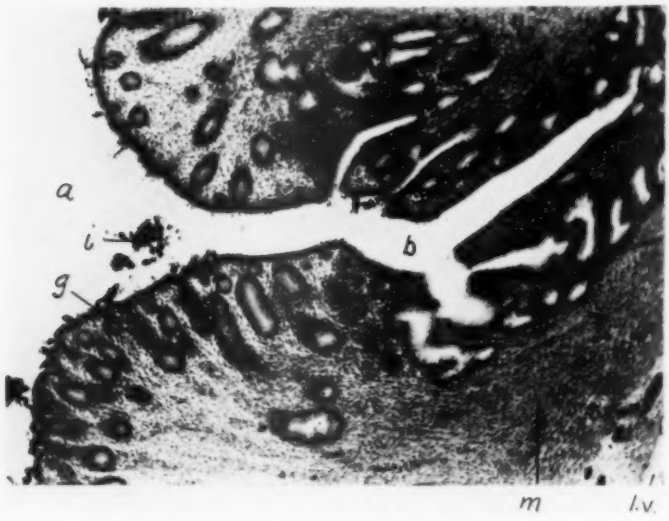

FIG. 13. × 100. Uterus of a lioness; a magnification of area *b* in Figure 12. Uterine glands, *g*, are at the very junction or tube, *b*, and uterus, *a*. The circular layer of plain muscle, *m*, is increased. Some of the injected ink, *i*, entered the tube. A few large lymph vessels, *l.v.*, were observed.

The histological sections showed that the tube joined the uterus obliquely (Figs. 12 and 13). There was only a slight elevation within the uterine cavity at the tubal ostium. Again the ciliated epithelium covering this region was slightly more columnar than that elsewhere in the uterine cavity, and in general resembled the tubal epithelium. Uterine glands were present almost to the very opening of the tube. Stroma cells were relatively few near the epithelial layer, but were more compact and were joined by fibrous connective tissue at the

muscle layer. Again the circular layer of plain muscle predominated at the tubo-uterine junction (Fig. 13). The blood supply to this region was very good. Lymph vessels were not numerous. The muscular layers and adventitia had large vessels (Fig. 13), whereas the stroma layer had only a limited lymph supply.

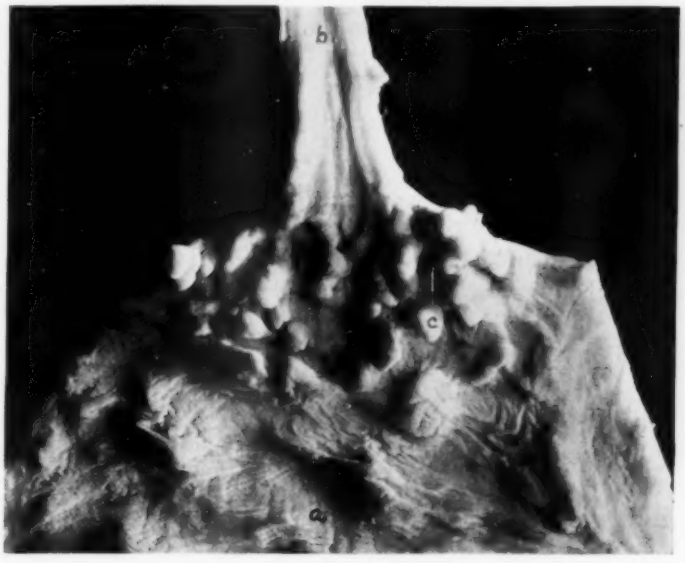

FIG. 14. × 4.6. Photograph of a dissection of the mucous coat at the tubo-uterine junction in the pig. At the junction of the tube, *b*, and the uterus, *a*, are seen numerous polyp-like projections, some of which, *c*, are sharply outlined, whereas others, *d*, are more flat and blend more readily with the uterine mucosa.

Pig. All the specimens of the sow's uterus were obtained in a fresh condition from a neighboring slaughter-house. With the unaided eye large polyp-like projections were seen guarding the tubal ostium and projecting into the uterine cavity. If the uterine cornu was injected with fixing fluid under pressure, then these projections appeared more flattened. An idea of these masses can be gained from figure 14 which was made from a specimen macerated in 30-per-cent

alcohol for 24 hours; the mucosa was then dissected off from the underlying muscular coat and the specimen pinned out on cork and fixed in formalin. It will be seen that the polypoid masses are distributed irregularly at the tubal ostium, and although about thirty-seven individual bulbous masses can be counted, several of them fre-

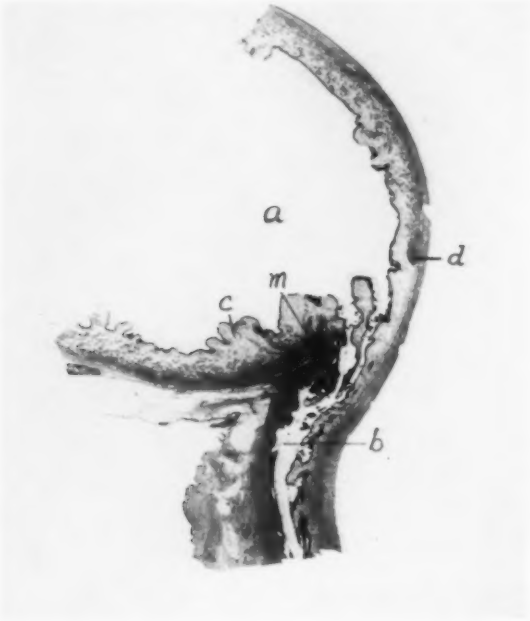

FIG. 15. × 5.5. Section of a pig's uterus, to show the oblique manner in which the tube, *b*, joins the uterus, *a*. Polyp-like projections, *c*, guard this communication. The circular muscle layer at *m* is well developed. Uterine glands do not extend beyond the point, *d*. In several instances, apparently due to the efficient closure of the tubal ostium by these polypous masses, the uterine wall was ruptured before any material injected into the uterine cavity escaped into the tube.

quently are on one stem. In general it will be noted that they are more numerous near the opening of the tube, and gradually become less peripherally in the uterine cavity. As a rule, the longitudinal folds within the tube terminated in one or more of these projections which

were usually not pedunculated. The polyps were frequently 2 mm. high.

The material for Figure 15 was taken from an adult sow whose right uterine cornu was injected with India ink, and it was not until a

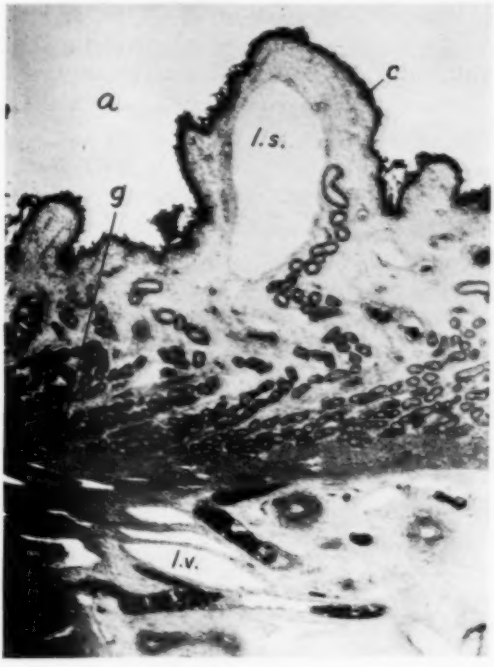

FIG. 16. × 38. Section of a pig's uterus near the tubal ostium to show the nature of the large lymph sinuses, *l.s.*, which frequently occupy a large part of a polypous projection, *c*. The axis of the uterine glands, *g*, is more oblique as the tube is reached. The uterine lumen is given as *a*. Numerous lymph vessels, *l.v.*, are in the muscular coat and adventitia.

pressure of 100 mm. of mercury was reached that any ink entered the tube. This figure illustrates very well the oblique angle at which the tube joins the uterus. The epithelium covering these polyp-like masses was slightly more columnar and also contained more cyto-

plasm than the epithelium elsewhere in the uterus; it resembled more the epithelium of the tube. Uterine glands were quite common in this general region and sections of such glands were frequently seen at the base of the polyps. The stroma layer was very loosely knit in the body of the polyp-like projections but became more compact at the base. The circular muscle layer was only slightly increased at the tubo-uterine junction, and the bulk of this increase was on the side of the tube which made the acute angle with the uterus. In fact, the musculature at this point was only slightly greater than that in the adjoining part of the tube. There was the usual good blood supply in this region. Of particular interest was the large amount of space occupied by the lymph system. Not only were the polypoid masses frequently almost completely filled by a lymph sinus (Fig. 16) but the entire stromal layer as well as the muscular coats and adventitia had large vessels. It is difficult to think of any tissue which shows a prettier lymphatic picture than that offered by this region.

LITERATURE AND DISCUSSION

Anatomically, not very much has been written on the tubo-uterine junction in lower animals. Bischoff in 1852 described very well the gradual transition of tube and uterus in the guinea-pig; but he did not note any mucous folds at this point. Allen, in 1922, mentioned valve-like folds which guarded the entrances of the oviduct into the uterine cornu of the mouse. The most recent account was that by Kelly, in 1927, who reconstructed the uretero-tubal junction in the guinea-pig and showed that numerous folds of mucosa guard the tubal ostium.

It is of course impossible to make generalizations on the morphology of the tubo-uterine junction from the material detailed above. However, except in the rat and guinea-pig, the tube joined the uterus at an angle near the apex of the cornu. This relationship was particularly obvious in the case of the pig and rabbit. For the guinea-pig Kelly stated that the uterine horn was a trumpet-like expansion of the tube which did not enter its wall obliquely. Taken by and large it seemed as if the tube were partly invaginated into the uterine cavity, and in favor of this view may be mentioned that the epithelium resembled more that of the tube, and that the muscular coats of the tube swept into the uterus for a short distance, *e.g.*, Figure 15, before they were

joined by the corresponding coats of the uterine wall. Again, uterine glands were absent at the junction in many of the animals, thus stressing a tubal characteristic.

The character of the mucous folds or polyp-like masses was not constant. There was a great difference, not only in size, between the large polypoid projections of the pig and rabbit and the relatively small folds in the rat and dog, but also in the number of these folds. As a rule, the folds were more developed on that side of the ostium which was nearer the apex of the cornu.

One feature was virtually constant for all animals, namely, the increase in the size of the sphincter muscle at the tubal ostium. In the mouse this musculature was scant. Possibly certain physiological changes in the uterus, such as pregnancy, caused an increase in this as well as the remaining muscular layer. Such a condition might explain the interesting ridge of musculature in the pregnant rabbit (Fig. 7) particularly so since the non-pregnant uterus of the same species did not show such a marked muscular development (Fig. 8).

The large lymph sinuses within the polypoid projections, particularly in the pig, were very unusual. The general morphology of these lymphatic vessels has recently been described by Andersen for the pig. Large lymph vessels were seen not only in the mucous folds, but also in the plain musculature and adventitia. The smaller the animal the fewer were the lymphatics; the lioness was an exception.

Physiologically, the tubo-uterine junction has received considerable study and speculation. Many investigators have found it difficult at times to inject the tubes from the uterus, but only a few have studied the anatomy of the region in order to find out a possible reason for the difficulty. Allen noticed that it was difficult to inject the oviducts from the uterus in the mouse, but he found that valve-like folds of the mucosa guarded the entrance of the oviduct into the uterine cornu, and thus there was an anatomical basis for the difficulty with the injection. He stated that the valves guarded against a back-flow of material into the tubes from a distended uterus. Examination of Figure 3 will readily explain why the mound-like folds will collapse and block the passage of material into the uterus, irrespective of the presence of a plain muscle sphincter in this region which need only play a minor part in the occlusion.

Other investigators, v. Mikulicz-Radecki, Lueg, and Nahmmacher, believed that a mechanism was present that prevented the transport of fluid from the uterine cornu into the tube of the rabbit. This mechanism they believed to be due to the ordinary pressure exerted by the normal peristaltic force of the tube in a direction which was towards the uterus. Not until this force was overcome by the pressure of the injection was any contrast fluid which was opaque to the roentgen ray forced into the tube. These authors made no histological study of the tubo-uterine junction and therefore were unable to consider the polypoid projections which surrounded the tubal ostium at this point (Figs. 6, 7 and 8). Undoubtedly the efficiency of the closure of the tube at this point was attested to by the fact that these authors did not find within the tube or peritoneal cavity any of their injection mass which had been colored with indigo-carmine and which had been allowed to remain in the uterus four hours under low pressure.

Also in 1926, Bondi, after studying the tube and uterus in the rabbit, advanced a different explanation for the fact that, when he tied off the uterine cornu, material from the resulting cystic extremity of the uterus did not enter the tube. He believed that the occlusion of the tube under such circumstances was due to its anatomical arrangement since it entered the uterine cornu obliquely and thus reminded one of the entrance of the ureter into the bladder. Accordingly, the greater the distention in the uterus, the greater would be the lateral pressure on the tube as it pierced the uterine wall. He studied the morphology of this region microscopically, and it is interesting to note that the large polyp-like folds at the tubal ostium apparently were of no significance in comparison with the course of the tube through the wall of the uterus.

That a sphincter might be responsible for the occlusion of the tube was considered by Schneider and Eisler in 1927. These authors injected iodipin into the uteri of women, and by means of the roentgen ray found in numerous instances a definite sphincter-like constriction at the uterine ostium of the tube. They believed that the sphincter-like contraction which they observed was due to the contraction of the well developed circular layer of plain muscle, and that the fluctuation in transuterine insufflation pressures as noticed by Guthmann were probably as much due to the contraction of this sphincter as to the peristalsis of the tube.

Rubin has recently stated that he was able to detect a spasm at the tubo-uterine junction in his peruterine insufflation tests for tubal patency. He recorded the pressure fluctuations on a smoked drum, and noticed that in such a case the initial pressure rose well above 100 mm. of mercury, usually from 150 to 180, even reached 200 mm., and then fell to 140 or less gradually, or it fell more sharply to a lower level when more or less typical fluctuations were evident. Whatever evidence Rubin had to substantiate the claim that such a curve was due to a spasm at the tubo-uterine junction only was not presented.

In connection with the Rubin test it will be recalled that Ferguson has reported a marked discrepancy in the pressures necessary for the insufflation in the same individual at different times. Whether this difference was due to the ordinary premenstrual swelling which might partially block the tubal ostium or whether it was due to a spasm of the sphincter at the tubo-uterine junction, or to both factors, was not discussed.

From a study of the musculature at the tubo-uterine junction in the laboratory animals as reported above, it seems reasonable to suppose that a sphincter action might be partly if not entirely responsible for an obstruction of the tube. In many animals this circular muscle layer was well developed, and together with such marked polyp-like projections as were observed, for example, in the pig and rabbit, the contraction of this muscle might approximate these projections and block the tubal opening very effectively. In this respect the polypoid masses might function in a manner similar to the Pförtnerschwulst of the pyloric portion of the pig's stomach in being an accessory sphincter structure, and be of particular use in pregnancy. In the case of the rabbit some of these masses were forced into the lumen of the tube (Fig. 6).

That this sphincter mechanism was effective was easily attested to by those experiments in the pig in which the wall of the uterus ruptured before any material was forced into the tube. Kelly ruptured the uterine horn in the guinea-pig on several occasions without injecting any material into the lumen of the tubes. In one instance he recorded a pressure of 504 mm. of mercury without any injection of the tube. That the uterine wall of the guinea-pig withstood such a pressure is equally remarkable.

In certain injections of the pig's uterus it was noticed that the tube on one side could be injected with relatively little pressure, whereas a corresponding injection on the opposite side was obtained only with much higher pressure.

Whether there is any relationship between the patency of the uterine ostium of the tube and the various stages in the oestrous cycle has apparently not been definitely determined as yet. Dyroff has considered a relationship between an internal secretion of the corpus luteum and a dilation sensitivity of uterus and tube as mediated by the involuntary nervous system. The patency of the tubal ostium in the pig may thus be determined not only by the tone of the muscular sphincter, but also by the size of the polypoid projections which may vary with the lymphatic engorgement.

As regards the human uterus, Kennedy in 1925 indicated the rôle which a spasm of the isthmic portion of the tube may cause. For example, a spasm of the tubo-uterine juction may be responsible for the pains associated with dysmenorrhea. Again, delayed conception or even sterility might be produced by the occlusion of the tube at its uterine ostium. Finally, it is possible that the entrance of the fertilized ovum into the uterine cavity might be blocked by a sphincter action at the tubo-uterine junction, and a tubal pregnancy be produced. Certain it is that the lumen of the tube at the uterine ostium is very small, and that the sphincter muscles here are well developed (Williams).

SUMMARY

A brief account has been given of the general morphology of the tubo-uterine junction in various animals. In the rabbit and pig there were numerous polyp-like projections visible to the unaided eye extending into the uterine cavity. Similar folds, but less in degree, were found in the mouse, rat, guinea-pig, and cat; in the dog and lioness they were developed the least. In all animals the circular layer of plain muscle fibers in this region was well developed and suggested a sphincter action, which, together with the mucous folds, might effectively shut off the tube. In fact, in several instances the uterine wall was ruptured before any injection mass escaped into the tube. The relationship of this mechanism to such physiological states as the

oestrous cycle and pregnancy, and to such pathological conditions as dysmenorrhea, sterility and ectopic pregnancy is considered briefly.

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THE SURFACE TENSION OF HUMAN BLOOD UNDER NORMAL AND PATHOLOGICAL CONDITIONS[1]

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INTRODUCTION

Within the past two decades a number of observations have been published concerning the surface tension of blood serum in various pathological conditions. Low values have been reported in conditions with jaundice, diseases of the liver, cancer, nephritis, uremia, circulatory disturbances, anxiety neurosis, pregnancy, eclampsia, and tuberculosis. On the other hand, high values have been mentioned in conditions associated with anemia.

The surface tension values to be found in the literature have varied considerably according to the various techniques employed for making the determinations. Nineteen of the more commonly used methods have been described by Ferguson (1), of which probably the most frequently employed has been the stalagnometric method of Traube (2). Recently du Noüy (3) has shown with the ring method that there is a spontaneous and rapid decrease of the surface tension of serum as a function of time, since adsorption takes place in the surface layer. After 2 hours the surface tension becomes practically constant because equilibrium has been established between the surface layer and the bulk of the solution. The difference between the initial value and the value after 2 hours he calls the time-drop.

The following series of observations have been made with the direct reading du Noüy tensiometer, showing the variations in the surface tension values with the time-drop.

METHOD OF STUDY

The procedure for the determinations of the surface tension of the blood serum and the method of collecting the blood have already been

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described (4). The initial readings were made within 1 to 3 hours after drawing the blood, and the second readings after the sera had stood undisturbed for two hours. Any sera showing even the slightest hemolysis were discarded, as hemolysis tended to lower somewhat the surface tension values, a fact previously observed by Kisch and Remertz (5). Every precaution described by du Noüy (3) (6) was scrupulously observed as to the cleaning of the glassware and the protection of the sera. All determinations were made at a temperature of 23° to 25°C. In every case the blood was collected after 15 hours of complete fast. Undiluted serum was used for all the observations, although du Noüy (7) states that for normal human serum the maximum drop is obtained in a dilution of 1:50,000. For the purpose of the present study, however, it was thought advisable to study the undiluted serum. With undiluted material less handling was required, thus lessening the chance for contamination.

A rather large number of observations were made comparing the surface tension values for serum with those for plasma, both from oxalated blood and from blood in which coagulation was prevented by heparin. It was found that the initial surface-tension values for plasma were several dynes higher than for serum. The time-drop, when using plasma, was slightly greater than when serum was used. Heparin and oxalate added to serum had no apparent effect on the tension values. Except for the time-drop, a similar phenomenon was observed by Gabbe and Simkowitz (8) using the stalagmometric method. These authors observed a few cases, however, in which plasma gave lower values than serum, a finding not observed in the present work.

In order to ascertain whether the presence of bile and its constituents, which are known to be highly surface active, could account for the lowered surface tension values observed in many instances, a quantitative estimation of the bilirubin content of the serum was made in almost every case according to the modification of the van den Bergh test recently described by McNee and Keefer (9). The value for the bilirubin content of the serum in the present study is expressed in milligrams per cent instead of in the unit (representing a dilution of 1:200,000) originally designated by van den Bergh, 0.5 mgm. per 100 cc. being the equivalent of 1 unit. The value for serum bilirubin in the average healthy individual was first reported by van den Bergh

(10) to be between 0.25 and 0.4 mgm. (0.5 to 0.8 units), but was reported in a later communication by him (11) to be between 0.1 to 0.25 mgm. (0.2 to 0.5 units). Lepehne (12) observed the average value in a series of patients not suffering from jaundice to be 0.15 mgm.

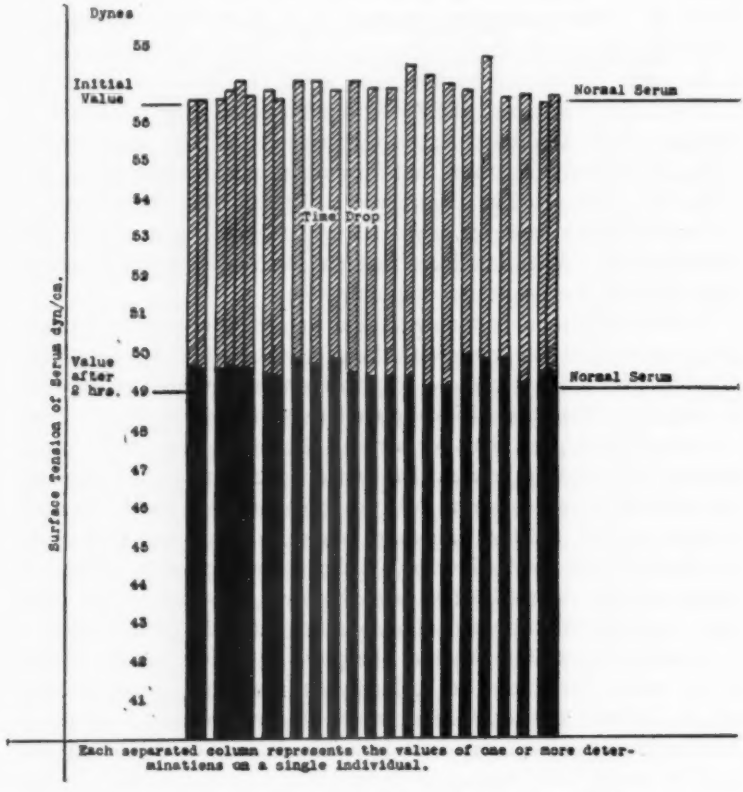
Dynes
Initial Value
Value after 2 hrs.
Surface Tension of Serum dyn/cm.
Time Drop
Normal Serum
Normal Serum
Each separated column represents the values of one or more determinations on a single individual.

FIG. 1. SURFACE TENSION OF SERUM. NORMAL PERSONS

The highest value for the upper limit of normal has been given by Greene and his co-workers (13) as 2.0 mgm. In the present paper 1 mgm. has been considered the upper limit of normal.

The cholesterol content of the serum was also determined in many

instances, because this substance has frequently been mentioned as a factor concerned in regulating surface tension. Determinations were made according to Sackett's modification of Bloor's method (14).

THE SERUM SURFACE TENSION IN NORMAL PERSONS

Table I and Figure 1 give the results obtained with the serum of 14 normal persons and also the results in 18 cases selected from patients on the wards and from the out-patient department. All of these persons were afebrile, without severe anemia and in fairly good general condition, so that a normal surface tension might be expected. From this series it is apparent that the initial surface-tension values of normal blood serum by the present technique may vary between 56.6 and 57.8 dynes and that the time-drop may vary from 6.9 to 8.2 dynes, equilibrium being reached at 48.9 to 49.9 dynes after standing two hours. Successive determinations in the same individual gave remarkably constant results.

NORMAL VARIATIONS DUE TO INGESTION OF MEALS

It seemed desirable to determine whether the ingestion of food, particularly food rich in lipoids, had any marked effect on the surface tension. Kisch and Remertz (5) have reported that they have observed that sera which were not quite clear and transparent, but more or less milky and chylous, showed a value below or just above the lower limit determined by them for normal sera. This fact is not surprising when one considers that the turbidity of sera, as is well known, is at least in part caused by a higher fatty content, and that neutral fat in emulsion is strongly surface active. However, Gabbe and Simkowitz (8) did not find such low values. They observed only a slight decrease of the surface tension or practically normal values following a meal rich in lipoids even when the sera showed considerable milkiness.

In our experiments three normal individuals of the staff were each given 250 cc. of 40 per cent cream, and two ward patients who were in good physical condition were given the usual ward noon-day meal. According to regular routine the blood was taken just before breakfast, at which time the individual had been fasting for 15 hours, and it was again taken $1\frac{1}{2}$ to 3 hours after the meal. The results of this series are shown in Table II. It will be seen that in the first 3 cases

1½ to 2 hours after the cream was given the serum appeared milky and there was a very slight decrease in the initial surface tension values. This decrease of the initial value varies from 0.7 to 1.4 dynes, and the decrease in the time-drop from 0.5 to 0.7 dyne. In regard to the two ward patients there was no change in the surface tension 1½ hours after the ward dinner, but there was a slight decrease 3½ hours after the meal, the decrease in the initial value varying from 1.2 to 1.5 dynes, and the decrease in the time-drop from 0.5 to 1.0 dyne.

We therefore conclude that the ingestion of lipoid-rich food has only a very slight effect in lowering the surface tension of blood serum.

SURFACE TENSION IN CONDITIONS WITH JAUNDICE

That bile decreases the surface tension of serum has long been known. Kascher (15) in 1907 reported that ligation of the bile-duct in animals produced, coincidently with the jaundice, a lowering of the surface tension of the blood serum. Similar reports have been found of lowering of the surface tension in jaundice and diseases of the liver by Traube (16), Neuberg (17), Schade (18), Aldersberg (19) and others.

Table III records a number of observations on patients with jaundice of varying degree. The findings in these cases are also shown graphically in Figure 2. It will be seen that most striking are the markedly diminished initial surface tension values and equally striking the low values after equilibrium has been reached. The time-drop varies greatly, ranging from 5.3 to 13.3 dynes, and shows marked contrast to the normal time-drop with the restricted range of 6.9 to 8.2 dynes. It will be seen that the more intense the jaundice, as measured by the van den Bergh reaction, the greater is the range of variation. It seems reasonable to suppose that this surface-tension effect is due to the bile salts present in the serum and that the amount of the latter is roughly proportional to that of the biliary pigments as indicated by the quantitative van den Bergh reaction.

In some conditions with jaundice, there is a slight increase in serum cholesterol. However, in the majority of the cases the cholesterol content is within normal limits. Neubauer (20), Adler (21) (22) and others consider cholesterol to be an important factor in the colloid complex of the bile acids affecting surface tension.

SURFACE TENSION IN MALIGNANT DISEASE

Low values of the surface tension of serum have been reported in cancer by Bauer (24), Bauer and Lasnitski (25), Solowiew (26), Aldersberg (19) and others. The significance of surface tension in the growth

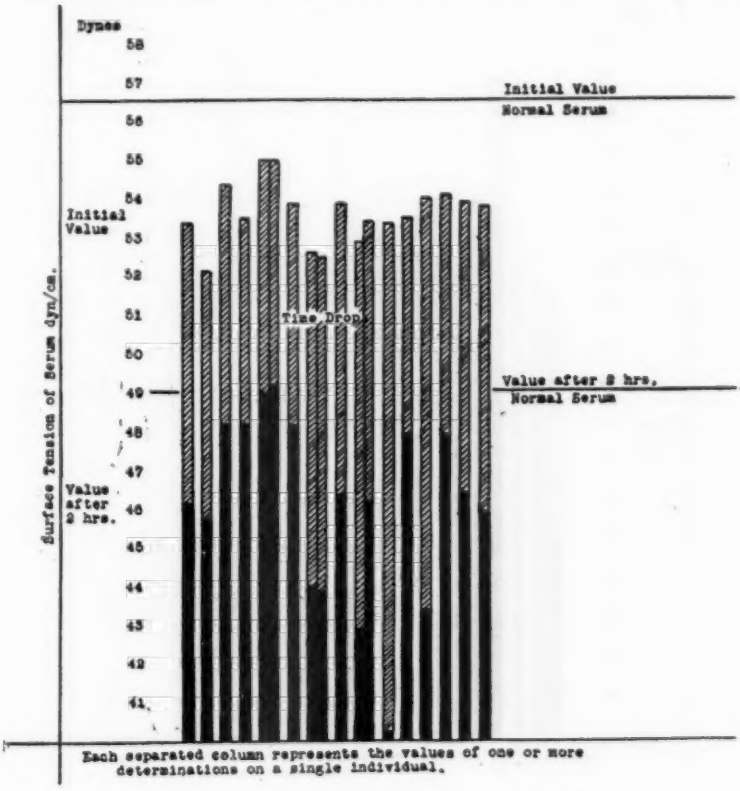

FIG. 2. SURFACE TENSION OF SERUM. JAUNDICE

of cancer is considered by Bauer to be extremely important, in that cell proliferation is greatly favored by a low tension. From Table IV it will be seen that in 20 cases of malignancy the surface tension values are low in all except two. If one rules out the cases in which there is

an increase in the bilirubin in the blood due to an obstructive jaundice from tumor pressure, or to an increase in bilirubin due to a latent icterus, the remaining cases still seem to show a slight decrease in the initial surface-tension values, but do not show a decrease in the equilib-

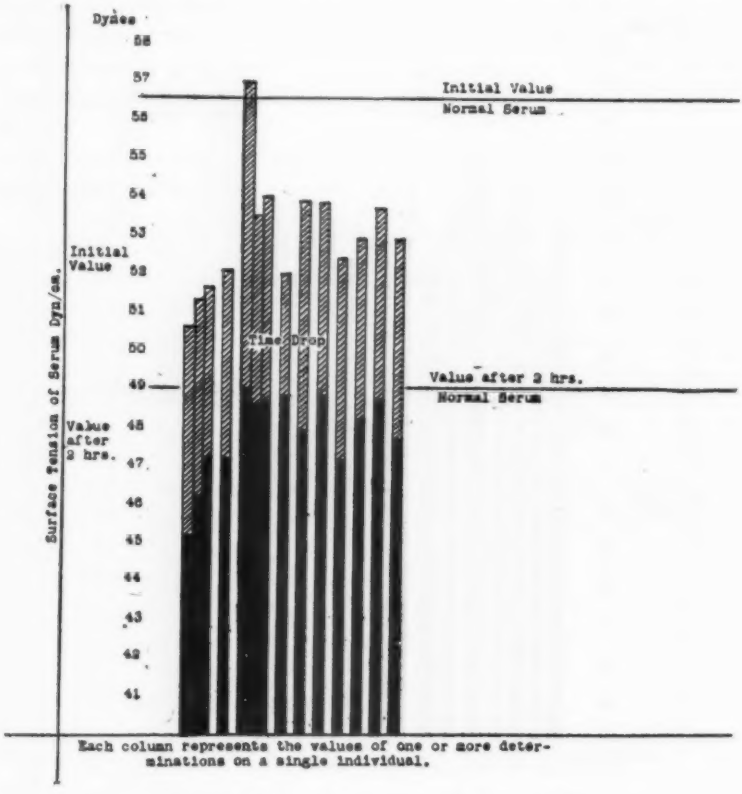

FIG. 3. SURFACE TENSION OF SERUM. PERNICIOUS ANEMIA

rium values as do the cases where there is increased bilirubin. Most of the patients studied were in an advanced stage with cachexia. No conclusions can therefore be drawn as to the surface tension in early malignancy, except that 2 cases gave normal values.

SURFACE TENSION IN NEPHRITIS

Uremia. Bickel (27) and Kascher (15) in 1905, using the stalagmometric method of Traube, found that uremia produced by the extirpation of the kidneys in animals was accompanied by a lowered

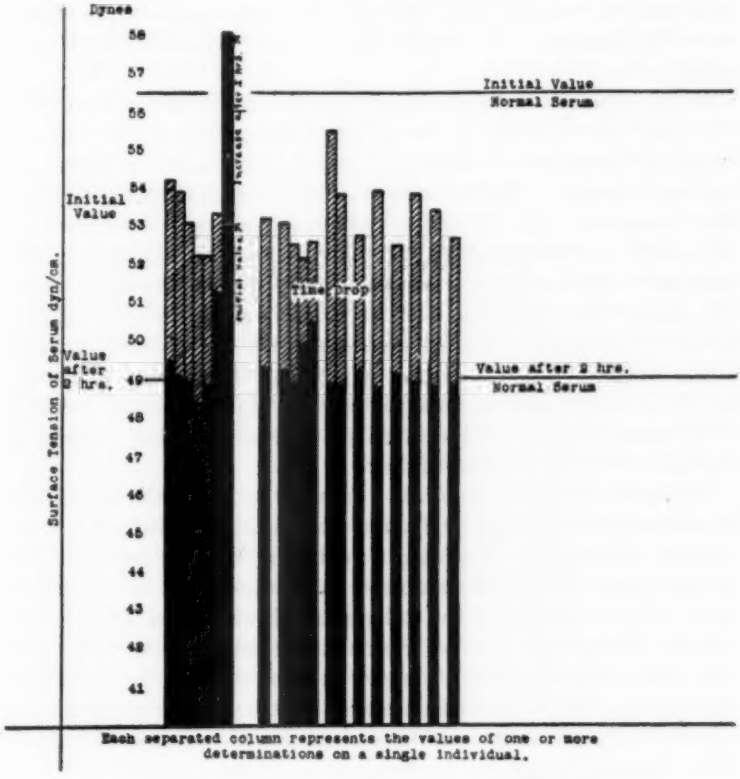

FIG. 4. SURFACE TENSION OF SERUM. UREMIA

surface tension of the blood serum, and that a fatal nephritis produced by the subcutaneous injection of uranium nitrate also produced a lowering of the serum surface tension. Kunoff (28) as well as Traube (29) have reported low surface tension in uremia. The low value in

uremia is considered by Traube to be due to the presence of some unknown surface active acid in the blood.

Table V gives the values in 10 cases of uremia. In all of them both the initial surface tension and the time-drop show a considerable decrease. The values are represented graphically in Figure 4 and show marked contrast to the normal values and to the values in the cases with jaundice. The time-drop in uremia varies from 2.1 to 6.7 dynes.

An interesting observation may be noticed in the case of Sarah W. The final determination on the serum of this patient showed an increase in the surface tension value after standing 2 hours, instead of the usual decrease. Examination of the serum in this instance showed that numerous, fine, refractive, needle-like crystals, identified as cholesterol, had precipitated in the clear serum while standing. The cholesterol content of the serum on this day was 454 mgm. per cent. The cholesterol value the week previous had been within normal limits. This precipitation of cholesterol was not observed in the serum from any other patient. As a rule the low surface tension values in uremia were not associated with high cholesterol content of the blood, but were found with high nitrogen retention. The sera in nearly all the cases appeared clear.

Nephrosis and diffuse nephritis. In many instances the low values in severe nephritis found by Traube were associated with milky sera. Clausen (30) by the drop-weight method of Harkins reported low surface tension in parenchymatous or tubular nephritis, as did Aldersberg (19) in nephrosis by the stalagmometric method of Traube, and recently Leiter (31) by the tensiometric method of du Noüy. In this study milky sera and low surface tension values were found in 3 cases of seemingly pure nephrosis and in 8 cases diagnosed as diffuse nephritis and associated with high blood lipoids. Of these 8 cases 4 were diagnosed clinically as acute and subacute nephritis and 4 as chronic diffuse nephritis. One of the acute cases progressed to a mild chronic form and 3 came to autopsy. The kidneys of these 3 cases showed tubular as well as glomerular changes. Of the 3 nephrosis patients 1 died. At autopsy the kidneys showed only tubular changes.

The surface tension values are given in Table V and are represented graphically in Figure 5. Attention may be called to the low initial

values and the persistent decrease in the time-drop. It is interesting that Leiter in his observations on nephrosis found, on the contrary, an increase in the time-drop with serum that was diluted 1:100. In the cases both of nephrosis and of diffuse nephritis the low surface tension values did not appear to have any relation to the extent of the edema.

An interesting phenomenon noticed in association with severe cases of nephritis was the rapid sedimentation of the red blood cells with the formation of the "buffy coat." In the uremia cases the blood clotted with a tough, gelatinous, yellowish layer at the top. When the edge of this layer was loosened from the sides of the centrifuge tube and the blood again centrifuged, clear serum rose to the top and in 10 to 15 minutes also clotted. This occurred 3 or 4 times before a pale clear fluid was obtained. In the nephrotic group, however, a "buffy coat" of milky-looking serum soon appeared after the blood was drawn, but successive clotting was not noticed. Rapid sedimentation of the red blood cells was noticed in association with low surface tension in many conditions other than nephritis and with normal surface tension values. Attention has been called to the tendency for rapid sedimentation to be associated with low surface tension by Gabbe and Simchowitz (8) and by Clausen (30) in his work on parenchymatous nephritis.

Acute nephritis and chronic nephritis of the arteriosclerotic type. In 4 cases of acute nephritis (at top of Table V) clear serum was found and the surface tension values were normal. In 10 cases of chronic nephritis of the arteriosclerotic type (see end of Table V) normal values were observed in about one half. However, several of the cases with low surface tension showed an increase in blood bilirubin.

The surface-tension values in association with other data on the above cases of nephritis may be referred to in another paper (40).

SURFACE TENSION IN CIRCULATORY DISTURBANCES

The findings in 10 patients with circulatory disturbances are given in Table VI. A lowering of the surface tension of the blood serum in severe disturbances of the circulation has been reported by Frei (32) and Schade (18). Clausen (30), however, reports only normal values in cardiac edema. Our observations agree with those of Clausen and

indicate that the surface-tension value in cardiac edema is not disturbed except when there is chronic passive congestion sufficiently severe to cause an increase of bilirubin in the blood. That an increase in the bilirubin content of the blood serum frequently occurs in myocardial insufficiency has been noted by a number of observers (10, 33, 34, 35, 36).

SURFACE TENSION IN ANEMIA

Pernicious anemia. In connection with the statements to be found in the literature regarding an increase in the surface tension in anemia (18) (19) it is interesting that in 10 cases of pernicious anemia (see Table VII) we have found a marked decrease in the surface-tension values. These values are represented graphically in Figure 3. It may be noticed that this chart has somewhat the appearance of that representing the jaundice cases, showing not only a decrease in the initial tension values, but also a rather wide range after equilibrium has been reached. In practically all the cases the final values are below the normal level.

In this series, as might be expected, a number of cases show an increase in serum bilirubin. There seems, however, to be no close correlation between the surface tension and the amount of bilirubin present in the serum, although there does seem to be a tendency to lower values both initial and after 2 hours when there is an accompanying hyperbilirubinemia.

Leukemia. The results of 5 cases of leukemia are also given in Table VII. In this group there is a definite decrease in the initial surface tension and a diminished time-drop, but the decrease is only slight and the equilibrium values are within normal limits.

Secondary anemia. In 3 cases of secondary anemia associated with a subacute bacterial endocarditis there are found slightly decreased values for the initial reading and the time-drop. Low tension values are found in anemia associated with malignant disease.

The observations recorded in Table VII illustrate the well-known fact that the cholesterol content of the serum in severe anemic conditions is invariably low. Aldersberg (19) attributes the high surface tension values which he observed in blood diseases as possibly due to this low cholesterol content of the blood. The present results

indicate that low serum cholesterol in both the primary and secondary anemias, by the present technique, is associated with low surface tension.

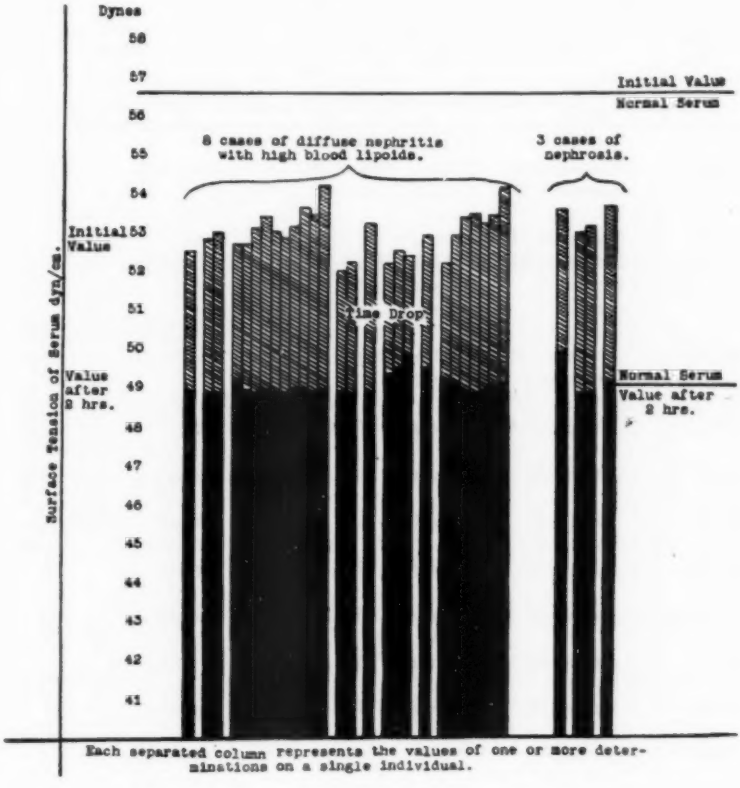

FIG. 5. SURFACE TENSION OF SERUM. NEPHRITIS

Polycythemia. Four cases of polycythemia examined are worthy of mention on account of the fact that in 3 of these low tension values were observed together with a diminished time-drop. In the fourth case normal values were found.

TABLE I

Surface tension in normal subjects. Temperature 23° to 25°C.

NAME AGE	DATE	APPEARANCE OF SERUM	SURFACE TENSION OF SERUM			REMARKS
			Initial reading	Reading after 2 hours	Time-drop	
			dynes	*dynes*	*dynes*	
G. H.	November 18	Clear	56.6	49.7	6.9	Staff
	November 27	Clear	56.6	49.6	7.0	
E. N.	November 18	Clear	56.6	49.6	7.0	Staff
	November 27	Clear	56.8	49.7	7.1	
	January 7	Clear	57.1	49.6	7.5	
	January 8	Clear	56.7	49.6	7.1	
E. H.	November 18	Clear	56.8	49.4	7.4	Staff
	December 1	Clear	56.6	49.3	7.3	
T. G.	November 18	Clear	57.1	49.8	7.3	Staff
A. S.	January 15	Clear	57.1	49.7	7.4	Student
H. P.	January 15	Clear	56.8	49.8	7.0	Student
C. W.	January 20	Clear	57.1	49.5	7.6	Student
I. T.	January 20	Clear	56.9	49.3	7.6	Student
S. W.	January 20	Clear	56.9	49.3	7.6	Student
L. W.	January 20	Clear	57.5	49.3	8.2	Student
E. T.	January 20	Clear	57.2	49.1	8.1	Student
W. S.	January 22	Clear	57.0	49.1	7.9	Student
J. B.	February 2	Clear	56.8	59.9	6.9	Student
E. C.	February	Clear	57.7	49.8	7.9	Student

TABLE I—*Continued*

NAME AGE	DATE	APPEARANCE OF SERUM	SURFACE TENSION OF SERUM			REMARKS
			Initial reading	Reading after 2 hours	Time-drop	
Miscellaneous conditions in which normal surface tension might be expected						
			dynes	*dynes*	*dynes*	
F. K. 24 W.	April 14	Clear	56.6	49.8	6.8	Undernutrition; hemoglobin 83 per cent (Sahli)
J. Y. 33 W.	March 23	Clear	56.7	49.2	7.5	Undernutrition; hemoglobin 86 per cent
P. L. 34 W.	January 27 February 2	Clear Clear	56.5 56.7	49.5 49.5	7.0 7.2	Mild hysteria
J. C. 49 C.	November 10	Clear	57.8	49.9	7.9	Incipient menopause
F. P. 61 W.	February 2 February 9	Clear Clear	56.9 56.8	49.4 49.4	7.5 7.4	Palsy
M. .M. 24 W.	November 24	Clear	56.9	49.4	7.7	Recovered coryza
F. Mc. 25 W.	January 14 January 21	Clear Clear	57.0 57.1	49.9 49.9	7.1 7.2	Arthritis deformans
R. S. 26 W.	January 14	Clear	57.5	49.5	8.0	Arthritis deformans
S. B. 49 W.	March 8 March 13	Clear Clear	56.6 56.8	49.3 49.3	7.3 7.5	Chronic arthritis; chronic adenoiditis
P. Mc. 48 W.	April 14	Clear	57.0	49.9	7.1	Chronic arthritis
B. H. 34 W.	May 9	Clear	56.5	49.5	7.0	Chronic arthritis
F. F. 18 W.	November 13	Clear	57.1	49.6	7.5	Second month of pregnancy

TABLE I—*Concluded*

NAME AGE	DATE	APPEARANCE OF SERUM	SURFACE TENSION OF SERUM			REMARKS
			Initial reading	Reading after 2 hours	Time-drop	
			dynes	*dynes*	*dynes*	
C. O. 37 W.	January 20	Clear	56.7	49.4	7.3	Psychoneurosis
J. M. 36 C.	February 23	Clear	56.5	49.6	6.9	Psychoneurosis; constipation
C. T. 18 W	April 14	Clear	56.9	49.4	7.5	Psychoneurosis
G. C. 33 W.	January 18	Clear	57.3	49.5	7.8	Convalescent pneumonia
C. T. 48 W	November 10	Clear	57.1	48.9	8.2	Disease of vestibular apparatus following fracture of skull
O. T. 67 W.	February 12 March 8	Clear Clear	56.5 56.8	49.2 49.3	7.3 7.5	Old gastric ulcer found at operation; hemoglobin 82 per cent

SURFACE TENSION IN HYPERTHYROIDISM

In 39 of 44 cases of hyperthyroidism, reported in a previous article (4), the initial surface tension was less than 56.6 dynes, and the time-drop in 38 of these cases was less than the minimal time-drop in the normal controls. Equilibrium was reached at a normal or just slightly less than normal value. An analogous phenomenon has been reported by Wilhelmj and Fleisher (37) in guinea-pigs, using the indirect reading du Noüy tensiometer. These authors found a decrease in the surface tension of the blood plasma of guinea-pigs after giving thyroid extract and thyroxin, and also found in these same animals an increase following thyroidectomy.

In the more severe cases of thyroid intoxication, low figures were found for the blood cholesterol in association with the low tension values.

SURFACE TENSION IN MISCELLANEOUS CONDITIONS

In the present study an effort was made to select cases in which there were no acute infections that might be a complicating factor in the study of the more chronic conditions. Nevertheless, three pa-

TABLE II

Surface tension in fasting and non-fasting conditions. Temperature 23° to 25°C.

	NAME	DATE	APPEARANCE OF SERUM	SURFACE TENSION OF SERUM			REMARKS
				Initial reading	Reading after 2 hours	Time-drop	
				dynes	*dynes*	*dynes*	
34	G. H.	November 27	Clear	56.6	49.6	7.0	Fasting
			Sl. milky	55.9	49.5	6.5	1½ hours after taking 250 cc. of 40 per cent cream
35	E. H.	December 1	Clear	56.6	49.3	7.3	Fasting
			Sl. milky	55.7	49.1	6.6	1¾ hours after taking 250 cc. of 40 per cent cream
36	E. N.	November 27	Clear	56.8	49.7	7.1	Fasting
			Milky	55.4	48.8	6.6	2 hours after taking 250 cc. of 40 per cent cream
37	C. J.	January 14	Clear	56.7	49.6	7.1	Fasting
			Sl. milky	55.8	48.7	7.1	2½ hours after noon dinner (ward)
38	P. L.	February 2	Clear	56.7	49.5	7.2	Fasting
			V. sl. milky	56.6	49.6	7.0	1½ hours after noon dinner
			Milky	55.5	48.8	6.7	3½ hours after noon dinner (ward)
39	F. P.	February 2	Clear	56.9	49.4	7.5	Fasting
			V. sl. milky	56.8	49.5	7.3	1½ hours after noon dinner
			Sl. milky	55.4	48.9	6.5	3½ hours after noon dinner (ward)

tients, Annie W. (Table VI) recovering from an acute inflammatory pelvic condition following an abortion, James C. (Table VIII) suffering from an attack of acute chorea, and Sarah W. (Table VI) who had an

TABLE III

Surface tension in conditions with jaundice. Temperature 23°–25°C.

NAME AGE	DATE OF EXPERIMENT	SURFACE TENSION OF SERUM			VAN DEN BERGH REACTION—SERUM BILIRUBIN	CHOLESTEROL	REMARKS
		Initial reading	Reading after 2 hours	Time-drop			
		dynes	*dynes*	*dynes*	*mgm. per 100 cc. blood*	*mgm. per 100 cc. serum*	
Herbert R. 23 W.	November 14, 1925	53.4	46.2	7.2			Infectious jaundice. Marked jaundice
Maurice S. 22 W.	November 14, 1925	52.1	45.7	7.4			Infectious jaundice. Marked jaundice
Philip N. 65 W.	December 5, 1925	54.3	48.2	6.1			Chronic cholecystitis and cholelithiasis. Moderate jaundice
Dora Q. 42 W.	December 23, 1925	53.5	48.2	5.3			Chronic cholecystitis and cholelithiasis. Moderate jaundice
George T.	January 10, 1926	55.0	49.0	6.0	2.0 (bi-phasic)	184	Mucous colitis. Icteric tint of skin and sclerae
27 W.	January 14, 1926	55.0	49.2	6.2	1.5		
Joyce B. 19 W.	January 9, 1926	53.8	48.2	5.6	0.5 (direct)	165	Infectious jaundice. Moderate jaundice

John B.	February 2, 1926	52.6	44.0	8.6	6.0 (direct)	315	Cholelithiasis (perforation of gallbladder). Marked jaundice
62 W.	February 16, 1926	52.5	43.8	8.8	6.8		
Marie T. 37 W.	March 8, 1926	53.8	46.6	7.2	0.5 (direct)	178	Cholecystitis and cholelithiasis. Syphilis (WaR). Moderate jaundice
Jannie S.	February 24, 1926	52.8	42.8	10.0	3.5 (direct)	208	Infectious jaundice; diabetes mellitus. Marked jaundice
40 W.	March 24, 1926	53.4	46.2	7.2	1.9		
Thomas P. 57 C.	April 8, 1926	53.4	40.1	13.3	28.3 (direct)	335	Reaction to arsphenamine; carcinoma of tongue. Marked jaundice
Addie S. 55 W.	April 28, 1926	53.5	47.9	5.6	2.4 (direct)	176	Cirrhosis of liver; ascites. Marked jaundice
Banks S. 42 W.	February 2, 1926	54.0	43.3	10.6	5.5 (direct)	333	Retroperitoneal tumor; syphilis (WaR). Jaundice
Byrd B. 64 C.	March 2, 1926	54.1	47.9	6.2	0.7 (direct)	287	Carcinoma of liver with metastases. Slight jaundice
John M. 42 W.	March 8, 1926	53.9	46.4	7.5	0.9 (direct)	250	Carcinoma of liver and carcinomatosis. Marked jaundice
Rufus R. 18 C.	January 25, 1927	53.8	45.9	7.9	1.0 (direct)	146	Retroperitoneal tumor. Bile in urine

TABLE IV

Surface tension in malignant disease. Temperature 23° to 25°C.

Appearance of serum clear in all cases

NAME AGE	DATE OF EXPERIMENT	SURFACE TENSION OF SERUM			VAN DEN BERGH REACTION—BILIRUBIN	CHOLESTEROL	REMARKS
		Initial reading	Reading after 2 hours	Time-drop			
		dynes	*dynes*	*dynes*	*mgm. per 100 cc. serum*	*mgm. per 100 cc. serum*	
John B. 51 C.	February 2, 1926 February 16, 1926	56.9 57.0	49.5 49.5	7.4 7.5	0.2 (indirect)	315	Carcinoma of liver; syphilis (WaR). Hemoglobin 64 per cent (Sahli)
Michael D. 65 W.	January 18, 1926	55.8	49.8	6.0	0.2 (indirect)		Carcinoma of colon. Hemoglobin 73 per cent. Died February 2, 1926. Autopsy
Lafe S. 45 W.	February 12, 1926	55.2	48.9	6.3	1.3 (indirect)	196	Mixed tumor of parotid with metastases. Hemoglobin 70 per cent. Died February 24, 1926. Autopsy
Mary D. 67 W.	January 5, 1926	55.4	49.2	6.2	1.2 (indirect)		Carcinomatosis. Hemoglobin 65 per cent
Byrd B. 64 C.	March 2, 1926	54.1	47.9	6.2	0.7 (direct)	276	Carcinoma with metastases to bone and lung. Died March 18, 1926. Autopsy
Myrtle J. 39 W.	February 23, 1926	53.6	48.8	4.8		169	Carcinoma of head of pancreas. Hemoglobin 84 per cent. Died February 28, 1926

Bertha O. 58 C.	February 25, 1926	54.5	49.0	5.5		220	Carcinoma of breast with metastases
John M. 42 W.	March 8, 1926	53.9	46.4	7.5	0.9 (direct)	184	Carcinoma of liver and carcinomatosis; syphilis; ascites. Hemoglobin 60 per cent. Died March 24, 1926. Autopsy
Ulysses Y. 32 C.	March 8, 1926 March 10, 1926	57.6 57.4	49.6 49.5	8.0 7.9	(Trace) (indirect)	238	Carcinoma of stomach, inoperable. Died March 20, 1926
Katherine D. 56 C.	March 8, 1926	54.3	49.0	5.3	0.3 (indirect)	246	Carcinoma of breast with metastases. Hemoglobin 75 per cent
Moses S. 65 C.	May 4, 1926	55.0	49.2	5.8		208	Carcinoma of pancreas with metastases to omentum; ascites. Hemoglobin 62 per cent. Died May 7, 1926. Autopsy
Samuel Mc. 43 W.	September 10, 1926	56.2	49.5	6.7		148	Carcinoma of stomach. Hemoglobin 44 per cent
Rachel K. 57 W.	January 4, 1927	55.6	49.8	5.8	2.7 (direct)		Carcinoma of liver with metastases. Hemoglobin 80 per cent
Arona S. 65 W.	November 24, 1926	55.3	48.8	6.5		387	Abdominal tumor with ascites and multiple metastases; arteriosclerosis. Hemoglobin 80 per cent
George M. 32 W.	December 18, 1925	53.2	49.0	4.2			Lymphosarcoma; syphilis; general anasarca. Hemoglobin 86 per cent

TABLE IV—*Continued*

NAME AGE	DATE OF EXPERIMENT	SURFACE TENSION OF SERUM			VAN DEN BERGH REACTION—BILIRUBIN	CHOLESTEROL	REMARKS
		Initial reading	Reading after 2 hours	Time-drop			
		dynes	*dynes*	*dynes*	*mgm. per 100 cc. serum*	*mgm. per 100 cc. serum*	
George S. 65 W.	January 22, 1926 January 29, 1926	53.6 53.5	47.6 47.6	6.0 5.9	0.5 (direct)	178	Lymphosarcoma of stomach. Hemoglobin 37 per cent. Autopsy
Banks S. 42 W.	February 2, 1926	54.0	43.4	10.6	5.5 (direct)	333	Retroperitoneal sarcoma; syphilis (WaR); jaundice. Hemoglobin 30 per cent. Died
Leon S. 14 W.	January 22, 1926	54.9	48.8	6.1	0.3 (indirect)	198	Sarcomatosis; sepsis (hemolytic streptococci). Hemoglobin 72 per cent. Died
Loney B. 50 C.	January 22, 1926	53.8	47.5	6.3	0.8 (direct)		Sarcomatosis. Jaundice. Hemoglobin 30 per cent. Died January 25, 1926. Autopsy
Rufus R. 18 C.	January 25, 1927	53.8	45.9	7.9	1.0 (direct)		Retroperitoneal sarcoma. Hemoglobin 52 per cent. Died February 7, 1927

acute upper respiratory tract infection, showed tension values for serum that were unusually high. In the case of Sarah W., however, the values, though within normal limits, were high when compared to subsequent successive determinations on the same patient. In these 3 cases, it will be noticed, there was an increase in the time-drop as well as in the initial value. However, the cases are too few from which to draw conclusions and are mentioned here only in view of the work of du Noüy (38) who observed an increased time-drop during the process of immunization in rabbits. This increase in the time-drop is believed by him to be a criterion for the presence of antibodies. Bauer (24), in his work on cancer, states that the surface tension of serum, by the stalagmometric method, is increased in cases with erysipelas, and believes that erysipelas temporarily retards cancer growth by causing an increase in the low tension often observed in carcinoma cases.

CONCLUSIONS

The surface tension of normal human blood serum, as measured by the tensiometric method of du Noüy, is remarkably constant both with regard to the initial value and the time-drop. Only a slight decrease in the initial surface tension and time-drop is caused by the ingestion of lipoid rich food.

Variations of the surface tension of the blood serum have been found to occur as follows:

a. Low surface tension with a variable time-drop ranging from less to considerably greater than normal appears to accompany hyperbilirubinemia due to jaundice; the more severe the jaundice as measured by the van den Bergh reaction, the greater the time-drop. Association of hyperbilirubinemia with hypocholesterolemia is found with low surface tension in pernicious anemia. Low surface tension in malignancy seems to be usually associated with an increase in serum bilirubin.

b. Low surface tension values and a persistent decrease in the time-drop are found in conditions where there exists a hypercholesterolemia and lipemia, as in nephrosis and some cases of diffuse nephritis.

c. In uremia low surface tension and a decreased time-drop is found in association with normal serum bilirubin and normal or slightly increased blood cholesterol.

TABLE V

Surface tension in nephritis. Temperature 23° to 25°C.

NAME AGE	DATE OF EXPERIMENT	APPEARANCE OF SERUM	SURFACE TENSION OF SERUM			VAN DEN BERGH REACTION—BILIRUBIN	CHOLESTEROL	NON-PROTEIN NITROGEN	EDEMA	CLINICAL DIAGNOSIS, REMARKS
			Initial reading	Reading after 2 hours	Time-drop					
			dynes	*dynes*	*dynes*	*mgm. per 100 cc. serum*	*mgm. per 100 cc. serum*	*mgm. per 100 cc.*		
Mike K. 31 W.	January 6, 1926 February 1, 1926 September 28, 1926	Clear Clear Clear	56.7 56.4 56.6	49.6 49.4 49.5	7.1 7.0 7.0	No increase	 219 223	 28	Marked general Slight general Slight general	Acute nephritis progressing to mild chronic form
Leonard S. 21W.	February 8, 1926 April 20, 1926	Clear Clear	57.1 56.9	49.5 49.5	7.6 7.4	No increase	204 195	35 34	Marked general None	Acute nephritis. Well
Paul S. 35 W.	January 28, 1926 February 3, 1926 February 16, 1926 March 8, 1926	Clear Clear Clear Clear	56.0 56.5 56.5 56.6	49.3 49.6 49.5 49.5	6.7 6.9 7.0 7.1	No increase	137 172 246 213	64 41 39 33	Marked general Rapid decrease Slight None	Acute nephritis. Well one year later except for trace albumin
Mildred L. 22 W.	February 28, 1926 April 19, 1926	Clear Clear	56.5	49.5	7.0	No increase	246 202	33 28	Moderate None	Acute nephritis. Well one year later
Ann T. 28W.	April 3, 1926 April 19, 1926	Clear Clear				No increase	213 192	30 28	Moderate None	Acute nephritis. Well one year later
Lorelle S. 32 W.	February 24, 1926 March 17, 1926	Clear Clear	56.5 56.0	49.5 49.5	7.0 6.5	No increase	230 244	38 59	Slight general Slight general	Acute-subacute nephritis progressing to chronic form
Flora W. 42 W.	April 10, 1926	Sl. milky	52.5	48.9	3.6	No increase	453	32	Moderate general	Acute nephritis. Died. Autopsy
Lillian P. 11 C.	April 3, 1926 April 13, 1926 April 15, 1926	Sl. milky Sl. milky Ascitic fluid	52.8 53.0 (53.5)	48.8 48.8 (50.2)	4.0 4.2 (3.3)	No increase	431 406 trace	56 68 88	Marked gereral No diminution	Acute and subacute nephritis. Died. Autopsy

John S. 34 W.	January 6, 1926	Milky	52.7	49.2	3.5	No increase			Marked general	Acute nephritis progressing to chronic form
	January 11, 1926	Milky	52.7	48.9	3.8		469	28	Rapid decrease	
	January 15, 1926	Milky	53.1	48.8	4.3		712			
	January 20, 1926	Milky	53.4	48.9	4.5			48	None	
	January 29, 1926	Milky	53.0	48.8	4.2		556		None	
	February 5, 1926	Milky	52.8	48.8	4.0		490	33	None	
	February 16, 1926	Milky	53.1	48.9	4.2		690		None	
	March 3, 1926	Milky	53.6	48.9	4.7		513	35	None	
	March 8, 1926	Milky	53.4	48.8	4.6		600		None	
	November 25, 1926	Opalescent	54.4	48.9	5.5		479	31	Slight	
Alvinia F. 15 W.	September 28, 1926	Milky	52.0	48.9	3.1		527	38	Marked general	Subacute and chronic diffuse nephritis.
	December 8, 1926	Sl. milky	52.2	48.8	3.4		484	35	persisting	Died. Autopsy. B. M. R. −28 to −35
Elmer B. 20 C.	December 9, 1926	Milky	53.2	48.8	4.4		682	73	Moderate	Acute nephritis; bronchopneumonia. Autopsy: subacute nephritis
John O 25 C.	January 12, 1926	Milky	52.2	49.3	2.9	No increase	937	56	Marked general	Chronic diffuse nephritis. No improve-
	January 18, 1926	Milky	52.5	49.5	3.0		867	68	Rapid decrease	ment
	January 27, 1926	Sl. milky	52.4	49.8	2.8		577	88	Recurrance	
Wm. G. 14 W.	November 16, 1925	Milky	52.9	49.5	3.4			44	Mild pitting edema	Chronic diffuse nephritis. Unimproved
Carrie Mc. 24 W.	November 14, 1925	Milky	52.2	49.2	3.0			30	Marked general	Chronic diffuse nephritis. Chronic course,
	November 24, 1925	Milky	52.9	49.1	3.9		756		Rapid decrease	developing arteriosclerosis and hyper-
	February 25, 1926	Milky	53.3	48.8	4.5	No increase	560		Slight	tension. B. M. R. −1
	March 17, 1926	Sl. milky	53.4	48.7	4.7		666	42	Slight	
	April 22, 1926	Sl. milky	53.2	48.8	4.4		635	47	Slight	
	September 1, 1926	Sl. milky	53.3	48.9	4.3		453		Slight	
	December 9, 1926	Clear	54.2	49.2	5.0		270	52	Slight	
Cecilia S. 9 W.	April 13, 1926	Sl. milky	53.5	48.9	4.6	No increase	465		Intermittent edema	Nephrosis, onset with acute nephritis
Emanual W. 9 W.	March 22, 1926	Sl. milky	52.9	48.8	4.1	No increase	420	23	Marked edema	Nephrosis. Died. Autopsy
	April 16, 1926	Clear	53.0	48.8	4.2		410		Slight edema	
Wm. L. 39 C.	September 1, 1926	Milky	53.4	49.2	4.2	No increase	388	29	Marked general Rapid decrease	Nephrosis. B. M. R. −20

TABLE V—*Continued*

NAME AGE	DATE OF EXPERIMENT	APPEARANCE OF SERUM	SURFACE TENSION OF SERUM			VAN DEN BERGH REACTION—DILIRUBIN	CHOLESTEROL	NON-PROTEIN NITROGEN	EDEMA	CLINICAL DIAGNOSIS, REMARKS
			Initial reading	Reading after 2 hours	Time-drop					
			dynes	*dynes*	*dynes*	*mgm. per 100 cc. serum*	*mgm. per 100 cc. serum*	*mgm. per 100 cc.*		
Wesley S. 37 W.	December 22, 1925	Clear	53.2	49.3	3.9		303	90	None	Chronic nephritis; uremia. Autopsy
Sarah W. 36 C.	November 19, 1925	Clear	54.2	49.5	4.7			152	Slight	Chronic nephritis; uremia
	November 24, 1925	Clear	53.9	49.1	4.1			151		
	December 12, 1925	Clear	53.1	49.0	4.1			119		
	December 22, 1925	Clear	52.2	48.3	3.9			100		
	January 4, 1926	Clear	52.2	48.8	3.4	No increase		119		
	January 18, 1926	Clear	53.4	51.3	2.1		197	135		
	January 22, 1926	Clear	53.1	58.1	(5.0)*		454	125		
Kate H. 36 C	November 21, 1925	Clear	53.1	49.2	3.9			197	None	Chronic nephritis; uremia. Autopsy
	November 24, 1925	Clear	52.6	49.8	2.8			221		
	November 30, 1925	Clear	52.2	49.8	2.4			140		
	December 2, 1925	Clear	52.6	50.6	2.0		313	282		
Oliver H. 53 C.	February 26, 1926	Clear	55.6	48.9	6.7	No increase	203	37	Moderate	Chronic nephritis; uremia. Autopsy
	April 18, 1926	Clear	53.8	48.8	5.0		243	80		
Emma T. 30 C.	February 17, 1926	Opalescent	52.7	49.2	3.5	No increase	315	189	None	Chronic nephritis; uremia. Autopsy
Olivia H. 32 C.	March 16, 1926	Clear	53.9	48.7	5.2	No increase	254	187	Slight pitting edema	Chronic nephritis; uremia. Died
James S. 42 C.	March 23, 1926	Clear	52.6	49.2	3.4	No increase	420	194	None	Chronic nephritis; uremia. Autopsy
Addie B. 52 C.	April 20, 1926	Clear	53.9	48. 9	4.0	0.4 (delayed)	196	37	Moderate	Chronic nephritis; uremia. Died

Eliz. D. 39 C.	August 24, 1926	Clear	53.4	48.8	4.6	No increase	326	122	Slight pitting edema	Chronic nephritis; uremia. Died
Eliz. J. 37 C.	December 9, 1926	Clear	52.6	48.8	3.8	No increase	297	232	Moderate	Chronic nephritis; uremia. Autopsy
Carmelite F. 27 W.	February 16, 1926 February 19, 1926	Clear Clear	53.3 53.7	48.9 49.2	4.4 4.5	No increase	172 166	37	Slight	Chronic nephritis; hypertension; arteriosclerosis
Ernest A. 35 W.	February 18, 1926	Clear	54.6	48.8	5.8	0.5 (direct delayed)	364	42	None	Chronic nephritis; hypertension; arteriosclerosis
George K. 60 W.	November 20, 1925	Clear	53.9	48.4	5.5	Jaundice color of serum		72	Considerable	Chronic nephritis; hypertension; arteriosclerosis
Frances H. 58 W.	January 20, 1926	Clear	56.5	49.6	6.9	No increase		39	None	Chronic nephritis; hypertension; arteriosclerosis
Eliz. F. 62 W.	January 22, 1926	Clear	55.4	48.7	6.7	Trace (direct delayed)	192	33	Slight	Chronic nephritis; hypertension; auricular fibrillation; arteriosclerosis
Jacob N. 53 C.	January 24, 1926	Clear	56.8	49.8	7.0	No increase	197	34		Chronic nephritis; arteriosclerosis
Maurice F. 39 C.	January 26, 1926	Clear	57.0	49.9	7.1	No increase	230	22	None	Chronic nephritis; arteriosclerosis
Fred M. 64 W.	January 29, 1926	Clear	56.0	49.6	6.4	No increase	221	43	Slight pitting edema	Chronic nephritis; arteriosclerosis
Wm. R. 52 W.	March 18, 1926 March 19, 1926	Clear Clear	54.4 54.3	48.7 48.5	5.7 5.8	No increase	103	43	Dependent edema	Chronic nephritis; splenomegaly; arteriosclerosis
Joseph Z. 49 W.	February 5, 1926	Clear	56.9	49.5	7.4	No increase	186	21	Pitting edema	Chronic nephritis; hypertension; arteriosclerosis

* Highly refractive chlolesterol crystals precipitated on standing causing rise instead of drop.

TABLE VI

Surface tension in circulatory disturbances. Temperature 23° to 25°C.

The appearance of the serum was clear in all determinations

NAME AGE	DATE OF EXPERIMENT	SURFACE TENSION OF SERUM			CHOLESTEROL	REMARKS
		Initial reading	Reading after 2 hours	Time-drop		
		dynes	*dynes*	*dynes*	*mgm. per 100 cc. serum*	
Nannie N. 45 W.	February 16, 1926	57.0	49.3	7.7	220	Myocardial insufficiency; auricular fibrillation; edema
Annie Y. 34 C.	February 25, 1926 March 16 1926	56.5 56.6	49.1 49.1	7.4 7.5	157 182	Myocardial insufficiency; enlarged liver; edema. Edema gone. Auricular fibrillation
Jacob N. 53 C.	January 24, 1926	56.8	49.8	7.0	197	Myocardial insufficiency; aortic defect; arteriosclerosis; no edema
Maurice F. 39 C.	January 26, 1926	57.0	49.9	7.1	230	Myocardial insufficiency; hypertension; arteriosclerosis; edema; hydrothorax
Charles H. 42 W.	January 26 1926 February 5, 1926	57.1 57.2	50.3 49.9	6.8 7.3	206	Myocardial insufficiency; aortic defect; no edema
Joseph Z. 49 W.	February 5, 1926 February 15, 1926	56.9 56.9	49.5 49.4	7.4 7.5	178	Myocardial insufficiency; hypertension; edema; tuberculosis of lungs; polycythemia
William D. 36 W.	March 15, 1926	56.9	49.6	7.3	192	Myocardial insufficiency; aortic defect; no edema

Blanch P. 28 W.	November 16, 1926 January 24, 1926	56.2 56.8	49.5 49.5	6.7 7.3		Chronic endocarditis (rheumatic); mitral defect; auricular fibrillation; cyanosis; edema (marked)
George K. 60 W.	November 20, 1925 December 12, 1925 December 14, 1925	53.9 53.9 54.0	48.4 48.2 48.2	5.5 5.7 5.8	 182	Myocardial insufficiency; chronic nephritis; hypertension; arteriosclerosis; marked edema of cardiac origin; enlarged liver. Van den Bergh not done
Bessie E. 52 W.	March 15, 1926	55.4	48.9	6.5		Chronic endocarditis (rheumatic); mitral defect; cardiac failure; cyanosis; splenomegaly; markedly enlarged liver. Van den Bergh test showed 3.3 mgm. bilirubin (indirect reaction)

Note: A Van den Bergh test was done in all cases with the exception of George K. Only 1 case showed an increase in serum bilirubin (Bessie E.) In the case of George K., however, in all three determinations the serum was noted as having a slight "jaundice" color.

TABLE VII

Surface tension in anemia. Temperature 23° to 25°C.

NAME AGE	DATE OF EXPERIMENT	APPEARANCE OF SERUM	SURFACE TENSION OF SERUM			VAN DEN BERGH REACTION—BILIRUBIN	CHOLESTEROL	REMARKS
			Initial reading	Reading after 2 hours	Time-drop			
			dynes	*dynes*	*dynes*	*mgm. per 100 cc. serum*	*mgm. per 100 cc. serum*	
Sam. M. 52 W.	January 7, 1926	Milky	50.6	45.2	5.4			Pernicious anemia. Hemoglobin 30 per cent (Sahli)
	January 15, 1926	Milky	51.3	46.2	5.0	Trace		
	January 26, 1926	Milky	51.9	47.2	4.7	(direct)	128	
Martha O. 43 W.	December 10, 1925	Sl. milky	52.1	47.2	4.9			Pernicious anemia. Hemoglobin 22 per cent
Sarah W. 61 W.	January 30, 1926	Clear	57.0	49.0	8.0		198	Pernicious anemia; adenoma of thyroid
	March 1, 1926	Clear	53.5	48.6	4.9	1.3 (indirect)	188	Hemoglobin 60 per cent
	March 7, 1926	Clear	54.0	48.7	5.3	1.3 (indirect)		
Robert D. 59 C.	March 23, 1926	Sl. milky	52.0	48.8	3.2	1.5 (indirect)	148	Pernicious anemia; arteriosclerosis; hemorrhagic retinitis. Hemoglobin 15 per cent
William T. 56 W.	April 8, 1926	Clear	53.9	47.9	6.0	2.3 (indirect)	144	Pernicious anemia. Hemoglobin 25 per cent

Augustus B. 53 C.	August 24, 1926	Clear	53.8	48.8	5.0	1.7 (indirect)	152	Pernicious anemia. Hemoglobin 44 per cent
Eliz. M. 39 W.	September 10, 1926	Clear	52.4	47.1	5.3	1.0 (indirect)	139	Pernicious anemia; syphilis (tertiary); leucoderma. Hemoglobin 37 per cent
Ben R. 61 W.	November 4, 1926	Sl. milky	52.8	48.2	4.6	0.7 (indirect)	135	Pernicious anemia. Hemoglobin 38 per cent
Lena D. 61 W.	November 4, 1926	Clear	53.7	48.6	5.1	Trace (direct)	148	Pernicious anemia. Hemoglobin 42 per cent
James Mc. 39 W.	November 11, 1926	Clear	52.9	47.7	5.2	0.5 (indirect)	186	Pernicious anemia. Hemoglobin 62 per cent
Mattie T. 60 W.	October 1, 1926	Clear	51.3	48.2	3.1	0.7 (indirect)	93	Acute myeloid leukemia; purpura hemorrhagica; bronchopneumonia. Hemoglobin 15 per cent
Eugene B. 24 C.	April 19, 1926	Sl. milky	56.1	49.6	6.5	No increase	89	Chronic myeloid leukemia
Laura S. 36 W.	April 8, 1926	Clear	55.9	50.0	5.9	No increase	109	Chronic myeloid leukemia
John K. 42 W.	March 8, 1926	Clear	55.4	49.3	6.1	No increase	163	Chronic lymphatic leukemia; leukemia of the skin
William S. 33 W.	April 21, 1926	Clear	55.8	49.5	6.3	No increase	159	Chronic lymphatic leukemia; purpura

TABLE VII—*Continued*

NAME AGE	DATE OF EXPERIMENT	APPEARANCE OF SERUM	SURFACE TENSION OF SERUM			VAN DEN BERGH REACTION—BILIRUBIN	CHOLESTEROL	REMARKS
			Initial reading	Reading after 2 hours	Time-drop			
			dynes	*dynes*	*dynes*	*mgm. per 100 cc. serum*	*mgm. per 100 cc. serum*	
Ottelia Z. 34 W.	January 8, 1926	Sl. opalescent	55.0	49.0	6.0		186	Secondary anemia; mitral defect; acute infection. Hemoglobin 51 per cent
Charles F. 26 W.	December 12, 1925	Clear	55.2	48.9	6.3		203	Sub-acute bacterial endocarditis; (Streptococcus viridans). Hemoglobin 54 per cent
Sophie P. 34 W.	January 12, 1926	Clear	55.1	49.2	5.9		172	Sub-acute bacterial endocarditis; Streptococcus viridans). Hemoglobin 52 per cent
Frank W. 33 C.	April 8, 1926	Clear	55.8	49.8	6.0	No increase	168	Sub-acute bacterial endocarditis; (Streptococcus viridans). Hemoglobin 50 per cent
Edna B. 40 W.	March 13, 1926	Clear	56.1	49.1	7.0	No increase	176	Marked emaciation. Hemoglobin 72 per cent
Annie W. 23 W.	March 26, 1925 April 2, 1926	Clear Clear	59.9 59.5	50.6 50.3	9.3 9.2	No increase	161	Secondary anemia; purpura; tuberculosis of lymph glands; excessive bleeding; acute infection

Catherine E. 42 W.	January 5, 1926 January 22, 1926 February 15, 1926	Sl. milky Sl. milky Sl. milky	52.3 52.6 52.8	48.6 48.7 48.4	3.7 3.9 4.4	 Trace (direct)	357 260	Polycythemia; hypertension. Hemoglobin 112 per cent. Before phenylhydrazine After phenylhydrazine
Estella C. 50 W.	March 15, 1926 March 22, 1926	Clear Clear	55.8 55.3	48.8 48.7	7.0 6.6	Faint trace (direct)	236	Polycythemia. Before phenylhydrazine After phenylhydrazine
Carrie T. 51 W.	March 15, 1926	Clear	55.2	49.0	6.2	No increase	380	Polycythemia; diabetes mellitus
Joseph Z. 49 W.	February 5, 1926	Clear	56.9	49.5	7.4	No increase	186	Polycythemia; hypertension; arteriosclerosis; myocardial insufficiency

TABLE VIII

Surface tension in conditions not previously mentioned. No increase in serum bilirubin. Temperature 23°–24°C.

NAME AGE	DATE OF EXPERIMENT	APPEARANCE OF SERUM	SURFACE TENSION OF SERUM			REMARKS
			Initial readings	Reading after 2 hours	Time-drop	
			dynes	*dynes*	*dynes*	
Eliz. S. 25 W.	December 10, 1925 December 14, 1925	Clear Clear	57.4 57.1	50.0 49.9	7.4 7.2	Diabetes mellitus, controlled, taking insulin
Walter P. 21 W.	December 10, 1925	Clear	57.6	50.1	7.5	Diabetes mellitus, controlled, taking insulin
Irene K. 16 W.	December 15, 1925	Clear	57.1	49.5	7.5	Diabetes mellitus, controlled, taking insulin
Bessie W. 13 C.	January 6, 1926	Clear	57.0	49.6	7.4	Diabetes mellitus, controlled, taking insulin
Henry K. 13 W.	December 18, 1925	Clear	57.4	49.6	7.4	Diabetes mellitus, controlled, taking insulin
Callie F. 57 W.	February 16, 1926	Clear	57.2	49.5	7.7	Diabetes mellitus, controlled, taking insulin
Birdie M. 49 W.	April 22, 1926	Clear	57.0	49.6	7.4	Diabetes mellitus, controlled, taking insulin

John T. 25 W.	April 8, 1926	Milky	55.1	49.0	6.1	Diabetes mellitus with acidosis, coma
Bessie W. 13 C.	April 11, 1926	Milky	55.4	49.1	6.3	Diabetes mellitus with acidosis and coma
Roy Mc. 24 W.	February 1, 1927	Clear	56.6	49.7	6.9	Renal glycosuria
Maud N. 45 C.	December 22, 1925	Clear	57.3	49.4	7.9	Diabetes insipidus
Peter K. 38 W.	January 14, 1926	Clear	57.1	50.0	7.1	Hodgkin's disease
Hattie H. 27 W.	January 20, 1926 January 27, 1926	Clear Clear	57.5 57.2	49.4 49.2	8.1 8.0	Hodgkin's disease; tracheal stenosis
Jay M. 39 W.	February 19, 1926	Clear	57.2	49.5	7.7	Hodgkin's disease
Isidore M. 23 W.	January 20, 1926	Clear	57.5	49.9	7.6	Hodgkin's disease
Carey J. 14 W.	January 14, 1926 January 27, 1926	Clear Clear	56.7 56.6	49.6 49.4	7.1 7.2	Scleroderma
Ogle N. 31 W.	January 22, 1926	Clear	57.0	48.8	8.2	Scleroderma
Alfred D. 36 W.	December 31, 1925	Clear	57.1	50.0	7.1	Multiple sclerosis

TABLE VIII—*Continued*

NAME AGE	DATE OF EXPERIMENT	APPEARANCE OF SERUM	SURFACE TENSION OF SERUM			REMARKS
			Initial readings	Reading after 2 hours	Time-drop	
			dynes	*dynes*	*dynes*	
Arthur S. 70 W.	February 12, 1926	Clear	57.0	49.1	7.9	Tabes dorsalis; syphilis
Eliz. M. 28 W.	October 1, 1926	Clear	56.8	49.9	6.9	Orthostatic albuminuria
Oscar D. 32 C.	November 26, 1925 December 4, 1926	Clear Clear	57.7 57.5	50.5 49.9	7.2 7.6	Alcohol poisoning. Edema Edema gone
Charles K. 37 W.	March 8, 1926	Clear	56.9	48.8	8.1	Acute alcoholism
James C. 13 W.	February 2, 1926	Clear	58.1	49.3	8.8	Acute chorea

d. In hyperthyroidism low surface tension is associated with a normal bilirubin value and a hypocholesterolemia.

3. In leukemia low surface tension and a decreased time-drop is observed with hypobilirubinemia and hypocholesterolemia.

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